GBX SEEDFIBER®

Microbiome-Boosting
Seed Powder*

amare®

TECHNICAL DATA SHEET

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GBX SEEDFIBER™

GBX SeedFiber™ is the next generation approach to optimizing the gut-brain axis. This phytobiotic rich formula contains seeds as sources of natural microbiome-boosting fibers, helping you feel fuller, longer.*

KEY INGREDIENTS

AHCC® — Active Hexose Correlated Compound of cultured mushroom mycelia extract that is rich in alpha-glucans. It is manufactured through an extended lipid culturing process that results in incredibly unique active components. It has over 30 human clinical studies, and is the #1 top immune support ingredient, with effects that help with innate and adaptive immune response.

- Studies have shown that AHCC® can reduce the production of glucocorticoids in case of stress. AHCC® also improves mood and energy in people suffering from chronic fatigue.
- AHCC® stimulates the activity of several types of immune cells: NK cells (involved in the defense against viral infections and cancer cells) and dendritic cells (regulate immune response).
- AHCC® favors immune function and improves our protection against various pathogens: Candida albicans, Pseudomonas, Staphylococcus aureus, Influenza virus, West Nile virus and Papillomavirus.
- AHCC® is beneficial for gut health; a study has demonstrated its capacity to reduce intestinal inflammation, and to favor the development of a healthy gut microflora (more Bifidobacteria, less Clostridium).

Cold-Pressed Seed Powder — Cold-pressed seeds are the most innovative process to attaining the most quality seed powder. Many companies use a heat-pressed process that exposes the seeds to heat and thermogenic profiles that alter the profile and quality of the seed. (The heat-pressed process provides MORE of the seed powder per seed at a lower quantity, and the cold-pressed seed powder provides substantially LESS of the seed powder per seed, but at a HIGHER quality.)

- **Sunflower Seed** — One of the top natural sources for good fats, copper, selenium, folate and vitamin E. Helps with cholesterol levels, bone health, heart health, detoxification, supporting skin and a good source of protein. Vitamin E and selenium help protect your cells from damage.
- **Cucumber Seed** — Great source of fiber and beta carotene, which helps with immunity, skin and eye health.
- **Cranberry Seed** — Good source of vitamin E, omega-3, -6 and -9, and also acts as a antioxidant to protect your body from stressors.
- **Concord Grape Seed** — Great natural source of vitamin A and E, which is crucial for skin, circulation, cholesterol, and has antioxidant effects.
- **Black Cumin Seed** — Boosts immune system, B vitamins and antioxidants.
- **Blackberry Seed** — Rich in omega-3 (alpha liolenic acid) and omega-6 (linoleic acid) fats good for heart and brain health.

CLINICAL STUDIES

Epilepsy Mikhailichenko N. Estimating Efficacy of AHCC as Immune Therapy for Patients Diagnosed With Pharmacoresistant Epilepsy. Presented at the 22nd International Congress on Nutrition and Integrative Medicine (ICNIM), July 2014.

Topic:

What effect does active hexose correlated compound (AHCC) supplementation have in patients diagnosed with pharmacoresistant epilepsy, to what degree is there a role in the immune system disease pathogenesis, and what is the efficacy of immune therapy?

Background:

Evidence of interaction between epilepsy and immunologic disorders has been growing over the last several decades. Clinical syndromes of secondary immunodeficiency have been found in 70–80% of cases involving mental patients with various severities of illness. Immunologic mechanisms may play a significant role in an integrated theory of epilepsy, and since infectious diseases such as ARVI, ENT diseases, urinary tract infections, and herpetic infections often attack patients with epilepsy, immune-correcting drugs have become a basis for treating these types of psychoimmunoneurological diseases. This study examined patients diagnosed with pharmacoresistant epilepsy and evaluated the effect of an immune-system role in pathogenesis of the disease and the efficacy of immune therapy using AHCC as a dietary supplement.

Study Type:

Human clinical intervention trial

Study Design:

Case studies of several children with pharmacoresistant epilepsy were examined using clinical methods. Immunologic tests were performed to assess clinical syndromes of secondary immunodeficiency and to identify multiple defects in the immune system. Immunologic examination was performed according to standard methods. Immune status was measured by percentage of T- and B lymphocytes in peripheral blood (total number of lymphocytes, percentage and absolute number of mature T cells (CD3+), T helpers (CD4+), and T killer-suppressors (CD8+), B lymphocytes (CD20+), and immunoregulatory balance between CD4+ and CD8+ concentrations. In addition, serum immunoglobulin A, G, and M (IgA, IgG, and IgM) were measured. All patients received combined treatment including base line antiepileptic and immune therapy using AHCC-2 for 1 month.

Subjects:

Several children

Dosage:

Not reported

Results:

Children with pharmacoresistant epilepsy had decreased mature T lymphocytes (CD3+) and T cells and an imbalance in the subset. The amount of CD3+ T lymphocytes in the epilepsy group was 42.42% ± 14.65%, which is 82.8% of average. The amount of CD4+ T lymphocytes was 71.6%, and cytotoxic CD8+ was 112.7%. The CD4+/CD8+ lymphocytes subset distribution and regulatory balance had a ratio of 1.28 ± 0.55, which was below average or only 58.6% of the average value. After AHCC intake, patients had positive changes of peripheral T cell pool (CD3+) and T helpers (CD4+). They also showed an improvement and increase in the ratio of T suppressors-killers (CD8+) to lymphocytes to 1.4. Due to increases in the CD4+ lymphocytes subset, the immunoregulatory balance of the CD4+ to CD8+ ratio improved. There was a 35% decrease of frequency and intensity of epileptic seizures. The patients' bodily health status and physiological functions also improved.

Conclusion "Patients with pharmacoresistant epilepsy have been found to have significant neuroimmune disorders, according to the results of immune cell testing. AHCC immunotherapy improves immune status by increasing the amount of T lymphocytes, by regulating the subset balance, and by activating phagocytes and humoral function. In addition, AHCC treatment decreased neurological immune dysfunction by regulating the amount of serum immunoglobulins, indicating a reversal of the autoimmune process that has significance in the development of epilepsy."

HPV Smith, Judith A., Pharm.D., BCOP, CPHQ, FCCP, FISOPP, Jonathan Faro, M.D., Yu Bai, M.D., Barbara Rech, RN, Anjali Gaikwad, M.S., MB (ASCP), Joseph A. Lucci III, M.D., Joseph A. Rodriguez, M.D., Teresa T. Byrd, M.D. Evaluation of Active Hexose Correlated Compound (AHCC) for the Eradication of HPV Infections in Women With HPV Positive Pap Smears. Presented at the 11th International Conference of the Society for Integrative Oncology, Houston, TX, October 26–28, 2014.

Topic:

Can women with HPV-positive Pap tests who don't show signs of abnormal cytology (abnormal cervical cells) and are treated with active hexose correlated compound (AHCC) undergo clearance of the infection?

Background:

HPV DNA has been detected in over 99% of cervical cancer patients. HPV infection is one of the most important predisposing factors of cervical cancer, though not the only one. HPV appears to be an important cofactor in the development of dysplasia and cancer, but it does not cause either condition by itself. Smoking, drinking alcohol, and a poor diet may also be important cofactors. There is currently no known effective medicine or supplement for eradication of HPV infections. Previously completed preclinical in vitro and in vivo mouse data that suggested AHCC will eradicate HPV in 16 out of 18 infections attributed this to the modulation of the expression and signaling of interferon alpha and beta. It was suggested that AHCC may help prevent subsequent HPV-related cervical cancers. The virus infects epithelial and mucosal surfaces and is a very common viral infection — 230 subtypes of HPV have been identified, including 100 human subtypes. Fifteen of the human HPV subtypes are carcinogenic and include the common subtypes: HPV 16, 18, 31, 39, and 41. According to the U.S. Centers for Disease Control and Prevention, several other cancers are related to HPV through sexual transmission, including 95% of anal cancer, 60% of oropharyngeal cancer, 65% of vaginal cancer, 50% of vulvar cancer, and 35% of penile cancer. The primary objective of the pilot study was to confirm the preclinical findings to determine whether AHCC is effective in eradicating HPV infections in women with negative-oncology Pap tests. AHCC is available over the counter as a nutritional supplement that functions by improving the innate immune system. Human and preclinical studies have shown that AHCC increases the number and/or activity of natural killer cells, dendritic cells, and cytokines. These help the body fight off infections, including those caused by viruses, and help block tumor growth.

Study Type:

Human intervention dose-finding pilot study

Study Design:

Case studies involving HPV-positive women treated orally with the extract AHCC once daily for up to 6 months. Patients who had documented persistent HPV-positive infections for greater than 2 years but were otherwise healthy and met the remaining eligibility criteria were enrolled in the study to evaluate the effectiveness of 3 grams of AHCC by oral administration to eradicate HPV. The regimen was repeated every month until the patient tested HPV negative or until 3 months of active treatment had elapsed. Patients who tested positive after 6 months of treatment were considered treatment failures. HPV testing

was completed with the Cervista® HPV HR Test (Hologic Inc., Bedford, MA) once a month, and a 2 mL blood sample was drawn for research purposes to monitor immune markers for response.

Subjects:

10 women with HPV-positive status

Dosage:

3 g, once a day on an empty stomach

Results:

Five subjects achieved a negative HPV test result — 3 with confirmed eradication after stopping AHCC — with the remaining 2 responders continuing on the study.

Conclusion:

"The preliminary results from this pilot study confirm previous preclinical findings that AHCC appears to be effective for elimination of HPV infections. These results will justify further reinvestigation. A formal phase 2 randomized, placebo-controlled study is underway at UTHealth–University of Texas Medical School at Houston."

Journal of Evidence-Based Complementary & Alternative Medicine Takanari J et al. Effects of Active Hexose Correlated Compound on the Seasonal Variations of Immune Competence in Healthy Subjects. 2015. Jan; 20(1):28–34.

Topic:

What is the effect of active hexose correlated compound (AHCC®) on immune competence in human subjects?

Background:

The immunocompetent cells include lymphoid cells (B cell, T cell, natural killer cell, etc.), granulocytic cells (eosinophil, neutrophil, basophil, etc.), and antigen-presenting cells (macrophage, monocyte, dendritic cell, etc.) and are affected by various factors including aging, stress, malnutrition, and various additional stressors. Seasonal changes can alter the immune function, especially with decreases of immune components during winter, which is evidenced by infectious diseases occurring more frequently in winter correlated with air temperature. The nasal airway is exposed to cold and cools down, reducing the mucociliary clearance and compromising the immune response of the nasal airway. In addition, sympathetic nervous activity is stimulated, increasing the number of granulocytes, and more adrenaline and noradrenaline are secreted from the adrenal gland. The number of natural killer cells decreases by adaptive response to low temperature in winter. This study evaluated the effects of active hexose correlated compound intake on immune competence in healthy volunteers.

Study Type:

Randomized, double-blind, parallel group, placebo-controlled human clinical intervention trial

Study Design:

Thirty-four subjects were randomized to receive placebo or AHCC for 4 weeks in early winter. All subjects took 4 capsules daily of active hexose correlated compound (250 mg/capsule) or placebo (250 mg dextrin only/ capsule) for 4 weeks between November and December. All subjects underwent peripheral blood testing and answered a questionnaire by the visual analog scale method. Natural killer cell activity was assessed by chromium-51 release assay to measure radioactivity. Immune score was done by lymphocyte subset analysis by a flow cytometric method for evaluating comprehensive immune strength by scoring various immune indexes, including the number of T cells, CD8þ and CD28þ T cells, naive T cells, B cells, natural killer cells, CD4/CD8 T cell ratio, and naive/memory T cell ratio. The complete blood count assessed for red blood cells, hemoglobin, hematocrit, platelets, white blood cells, and differential counts of white blood cells (neutrophil, lymphocyte, monocyte, eosinophil, and basophil).

Subjects:

34 subjects.

Dosage:

1 g/day delivered orally

Results:

Natural killer cell activity significantly increased in both groups during the study period. The natural killer cell number, however, was not altered in the active hexose correlated compound group, while the placebo group showed remarkable decline. In addition, the score of immunological vigor, an index of total immune competence, was maintained in the AHCC group, although that of the placebo group

decreased during the test period.

Conclusion:

"The results suggest that continuous use of AHCC maintained immune competence against seasonal changes during winter."

Healthy Adults Nutrition and Cancer Terakawa N, Y Matsui, S Satoi, H Yanagimoto, K Takahashi, T Yamamoto, J Yamao, S Takai, AH Kwon, Y Kamiyama. Immunological Effect of Active Hexose Correlated Compound (AHCC) in Healthy Volunteers: A Double-Blind, Placebo-Controlled Trial. 2008. 60(5):643–651.

Topic:

Does AHCC (active hexose correlated compound) have an effect on immune responses in healthy volunteers?

Background:

Biological response modifiers (BRMs) are substances that stimulate the body's response to infection and disease. Attempts have been made to treat cancer with BRMs, but their clinical efficacy has not been clearly confirmed. AHCC has had numerous positive clinical results on cancer patients without any adverse effects but has not been investigated for its effect on immune response in humans.

Study Type:

Human clinical intervention trial

Study Design:

Double-blind, randomized, placebo-controlled: Subjects were treated with AHCC daily for 4 weeks. Researchers took blood samples at base line and again after 4 weeks. The number of circulating dendritic cells (both DC1 and DC2 cells), natural killer cells, and CD4+/ CD8+ T lymphocytes was measured by flow cytometry. In addition, other immune function parameters were measured.

Subjects:

21 healthy volunteers

Dosage:

3 g of AHCC per day (n = 10) or placebo (n = 11)

Results:

Volunteers supplemented with AHCC had the following significant changes: • Greater number of total DCs than at base line and compared with control. • The number of DC1 cells was greater after AHCC intake than at base line, and the AHCC group had a tendency to have higher DC1s than control. • DC2s were significantly increased after 4 weeks compared with control. • The allo-stimulatory activity of DC1s was also increased after intake compared with control as measured by the mixed lymphocyte reaction.

Conclusion:

"These results suggest that AHCC could be an effective modulator of immunological function in patients with cancer. AHCC acts as a promising BRM."

Healthy Adults Journal of Nutritional Science and Vitaminology Spierings E, H Fujii, B Sun, T Walshe. A Phase 1 Study of the Safety of the Nutritional Supplement Active Hexose Correlated Compound, AHCC, in Healthy Volunteers. 2007. Dec; 53(6):536–539.

Topic:

Is AHCC (active hexose correlated compound) safe and tolerable in healthy subjects?

Background:

AHCC has been used for many years as a dietary supplement to enhance the immune system and in clinical trials as adjunctive treatment in hepatocellular cancer. Its safety has been previously based on anecdotal reports and its use in clinical practice. Phase 1 clinical trials are used to make the initial safety assessment of compounds with potential medical uses.

Study Type:

Human clinical intervention trial.

Study Design:

Phase 1 clinical trial: Subjects were treated with AHCC daily for 14 days. Laboratory data were obtained at base line and after 14 days of exposure to AHCC, and adverse events were monitored by a nondirected review of systems questionnaire 3 times during the trial.

Subjects:

26 healthy male or female subjects between 18 and 61 years of age.

Dosage:

9 g of AHCC per day (liquid form)

Results:

Laboratory results and adverse events were reported as follows: • 2 subjects (7%) dropped out because of nausea and intolerance of the liquid. • Nausea, diarrhea, bloating, headache, fatigue and foot cramps occurred in a total of 6 subjects (20%) but were mild and transient. • There were no laboratory abnormalities.

Conclusion:

“The adverse effects of 9 grams of liquid AHCC per day, a higher dose than used in routine clinical applications, are minimal and the dose was tolerated by 85% of the subjects. This trial supports the anecdotal evidence that AHCC is a safe supplement in clinical practice and that the side effects are generally mild and tolerable."

Gastric & Colon Cancer Natural Medicine Journal Kawaguchi Y. Improved Survival of Patients With Gastric Cancer or Colon Cancer When Treated With Active Hexose Correlated Compound (AHCC): Effect of AHCC on Digestive System Cancer. 2009. September;1(1):1–6.

Topic:

Does AHCC (active hexose correlated compound) have an effect on the survival rate of patients with gastric cancer or colon cancer?

Background:

Gastric cancer is the second-most-common cause of cancer death and colorectal cancer is the third-most-commonly diagnosed cancer worldwide. Current treatment options include surgical resection and/or chemotherapy regimes. However, both forms of cancer have poor survival rates. The 5-year survival for patients with unresectable metastatic colon cancer is less than 10%, and gastric cancer has an estimated age-adjusted survival rate of 33–44% in the United States and 51–54% in Japan. Tumor immunotherapy may provide another therapeutic option in an integrated approach. AHCC has demonstrated immune-stimulating activity and may be a potent biological response modifier (BRM) in cancer therapy.

Study Type: Observational study

Study Design:

Prospective cohort study: Patients with a histopathological diagnosis of gastric or colon cancer were recruited to receive oral AHCC as a postoperative adjunctive therapy in conjunction with standard chemotherapy. The cumulative survival rates for gastric and colon cancer patients were analyzed by KaplanMeier method.

Subjects:

132 patients diagnosed with gastric cancer, 113 patients diagnosed with colon cancer

Dosage:

For Stage 1, 2, or 3 patients: 3 g of AHCC per day (1 g three times per day); for Stage 4 patients: 6 g of AHCC per day (2 g three times per day)

Results:

AHCC supplementation resulted in the following difference in survival rates: • Improved cumulative 5-year survival rates for patients with gastric cancer (Stage 1A to Stage 3A) compared with other Japanese institutions • Improved cumulative 5-year survival rates for patients with colon cancer (Stage 2 to Stage 3A) compared with other Japanese institutions

Conclusion:

“AHCC is a potent BRM that may improve survival in patients with early stage gastric or colon cancer and warrants further investigation as an adjunctive immunotherapeutic in gastric and colon cancer treatment.”

Proc Natl Acad Sci U S A. 2011 Sep 20;108(38):16050-5.

Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve.

Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, Bienenstock J, Cryan JF.

Abstract

There is increasing, but largely indirect, evidence pointing to an effect of commensal gut microbiota on the central nervous system (CNS). However, it is unknown whether lactic acid bacteria such as Lactobacillus rhamnosus could have a direct effect on neurotransmitter receptors in the CNS in normal, healthy animals. GABA is the main CNS inhibitory neurotransmitter and is significantly involved in regulating many physiological and psychological processes. Alterations in central GABA receptor expression are implicated in the pathogenesis of anxiety and depression, which are highly comorbid with functional bowel disorders. In this work, we show that chronic treatment with L. rhamnosus (JB-1) induced region-dependent alterations in GABA(B1b) mRNA in the brain with increases in cortical regions (cingulate and prelimbic) and concomitant reductions in expression in the hippocampus, amygdala, and locus coeruleus, in comparison with control-fed mice. In addition, L. rhamnosus (JB-1) reduced GABA(Aα2) mRNA expression in the prefrontal cortex and amygdala, but increased GABA(Aα2) in the hippocampus. Importantly, L. rhamnosus (JB-1) reduced stress-induced corticosterone and anxiety- and depression-related behavior. Moreover, the neurochemical and behavioral effects were not found in vagotomized mice, identifying the vagus as a major modulatory constitutive communication pathway between the bacteria exposed to the gut and the brain. Together, these findings highlight the important role of bacteria in the bidirectional communication of the gut-brain axis and suggest that certain organisms may prove to be useful therapeutic adjuncts in stress-related disorders such as anxiety and depression.

Cell Mol Life Sci. 2013 Jan;70(1):55-69. doi: 10.1007/s00018-012-1028-z. Epub 2012 May 27.

Voices from within: gut microbes and the CNS.

Forsythe P, Kunze WA.

Abstract

Recent advances in research have greatly increased our understanding of the importance of the gut microbiota. Bacterial colonization of the intestine is critical to the normal development of many aspects of physiology such as the immune and endocrine systems. It is emerging that the influence of the gut microbiota also extends to modulation of host neural development. Furthermore, the overall balance in composition of the microbiota, together with the influence of pivotal species that induce specific responses, can modulate adult neural function, peripherally and centrally. Effects of commensal gut bacteria in adult animals include protection from the central effects of infection and inflammation as well as modulation of normal behavioral responses. There is now robust evidence that gut bacteria influence the enteric nervous system, an effect that may contribute to afferent signaling to the brain. The vagus nerve has also emerged as an important means of communicating signals from gut bacteria to the CNS. Further understanding of the mechanisms underlying microbiome-gut-brain communication will provide us with new insight into the symbiotic relationship between gut microbiota and their mammalian hosts and help us identify the potential for microbial-based therapeutic strategies to aid in the treatment of mood disorders.

Pre-Biotic Blend – Selected Background Documents

Brain Behav Immun. 2016 Feb;52:120-31. doi: 10.1016/j.bbi.2015.10.007.

Prebiotic administration normalizes lipopolysaccharide (LPS)-induced anxiety and cortical 5-HT2A receptor and IL1-β levels in male mice.

Savignac HM1, Couch Y2, Stratford M3, Bannerman DM4, Tzortzis G1, Anthony DC2, Burnet PW5.

Abstract

The manipulation of the enteric microbiota with specific prebiotics and probiotics, has been shown to reduce the host's inflammatory response, alter brain chemistry, and modulate anxiety behaviour in both rodents and humans. However, the neuro-immune and behavioural effects of prebiotics on sickness behaviour have not been explored. Here, adult male CD1 mice were fed with a specific mix of non-digestible galacto-oligosaccharides (Bimuno®, BGOS) for 3 weeks, before receiving a single injection of lipopolysaccharide (LPS), which induces sickness behaviour and anxiety. Locomotor and marble burying activities were assessed 4h after LPS injection, and after 24h, anxiety in the light-dark box was assessed. Cytokine expression, and key components of the serotonergic (5-Hydroxytryptamine, 5-HT) and glutamatergic system were evaluated in the frontal cortex to determine the impact of BGOS administration at a molecular level. BGOS-fed mice were less anxious in the light-dark box compared to controls 24h after the LPS injection. Elevated cortical IL-1β concentrations in control mice 28 h after LPS were not observed in BGOS-fed animals. This significant BGOS×LPS interaction was also observed for 5HT2A receptors, but not for 5HT1A receptors, 5HT, 5HIAA, NMDA receptor subunits, or other cytokines. The intake of BGOS did not influence LPS-mediated reductions in marble burying behaviour, and its effect on locomotor activity was equivocal. Together, our data show that the prebiotic BGOS has an anxiolytic effect, which may be related to the modulation of cortical IL-1β and 5-HT2A receptor expression. Our data suggest a potential role for prebiotics in the treatment of neuropsychiatric disorders where anxiety and neuroinflammation are prominent clinical features.

Br J Nutr. 2015 Aug 28;114(4):586-95. doi: 10.1017/S0007114515001889. Epub 2015 Jul 28.

Influence of galacto-oligosaccharide mixture (B-GOS) on gut microbiota, immune parameters and metabonomics in elderly persons.

Vulevic J, Juric A, Walton GE, Claus SP, Tzortzis G, Toward RE, Gibson GR.

Abstract

It is recognised that ageing induces various changes to the human colonic microbiota. Most relevant is a reduction in bifidobacteria, which is a health-positive genus. Prebiotics, such as galacto-oligosaccharides (GOS), are dietary ingredients that selectively fortify beneficial gut microbial groups. Therefore, they have the potential to reverse the age-related decline in bifidobacteria and modulate associated health parameters. We assessed the effect of GOS mixture (Bimuno (B-GOS)) on gut microbiota, markers of immune function and metabolites in forty elderly (age 65-80 years) volunteers in a randomised, double-blind, placebo (maltodextrin)-controlled, cross-over study. The intervention periods consisted of 10 weeks with daily doses of 5·5 g/d with a 4-week washout period in between. Blood and faecal samples were collected for the analyses of faecal bacterial populations and immune and metabolic biomarkers. B-GOS consumption led to significant increases in bacteroides and bifidobacteria, the latter correlating with increased lactic acid in faecal waters. Higher IL-10, IL-8, natural killer cell activity and C-reactive protein and lower IL-1β were also observed. Administration of B-GOS to elderly volunteers may be useful in positively affecting the microbiota and some markers of immune function associated with ageing.

Psychopharmacology (Berl). 2015 May;232(10):1793-801. doi: 10.1007/s00213-014-3810-0. Epub 2014 Dec 3.

Prebiotic intake reduces the waking cortisol response and alters emotional bias in healthy volunteers.

Schmidt K, Cowen PJ, Harmer CJ, Tzortzis G, Errington S, Burnet PW.

Abstract

RATIONALE:

There is now compelling evidence for a link between enteric microbiota and brain function. The ingestion of probiotics modulates the processing of information that is strongly linked to anxiety and depression, and influences the neuroendocrine stress response. We have recently demonstrated that prebiotics (soluble fibres that augment the growth of indigenous microbiota) have significant neurobiological effects in rats, but their action in humans has not been reported.

OBJECTIVES:

The present study explored the effects of two prebiotics on the secretion of the stress hormone, cortisol and emotional processing in healthy volunteers.

METHODS:

Forty-five healthy volunteers received one of two prebiotics (fructooligosaccharides, FOS, or Bimuno®-galactooligosaccharides, B-GOS) or a placebo (maltodextrin) daily for 3 weeks. The salivary cortisol awakening response was sampled before and after prebiotic/placebo administration. On the final day of treatment, participants completed a computerised task battery assessing the processing of emotionally salient information.

RESULTS:

The salivary cortisol awakening response was significantly lower after B-GOS intake compared with placebo. Participants also showed decreased attentional vigilance to negative versus positive information in a dot-probe task after B-GOS compared to placebo intake. No effects were found after the administration of FOS.

CONCLUSION:

The suppression of the neuroendocrine stress response and the increase in the processing of positive versus negative attentional vigilance in subjects supplemented with B-GOS are consistent with previous findings of endocrine and anxiolytic effects of microbiota proliferation. Further studies are therefore needed to test the utility of B-GOS supplementation in the treatment of stress-related disorders.

FEMS Microbiol Ecol. 2017 Feb;93(2). pii: fiw233. Epub 2016 Nov 16.

In vitro fermentation of B-GOS: impact on faecal bacterial populations and metabolic activity in autistic and non-autistic children.

Grimaldi R, Cela D, Swann JR, Vulevic J, Gibson GR, Tzortzis G, Costabile A.

Abstract

Children with autism spectrum disorders (ASD) often suffer gastrointestinal problems consistent with imbalances in the gut microbial population. Treatment with antibiotics or pro/prebiotics has been postulated to regulate microbiota and improve gut symptoms, but there is a lack of evidence for such approaches, especially for prebiotics. This study assessed the influence of a prebiotic galactooligosaccharide (B-GOS) on gut microbial ecology and metabolic function using faecal samples from autistic and non-autistic children in an in vitro gut model system. Bacteriology was analysed using flow cytometry combined with fluorescence in situ hybridization and metabolic activity by HPLC and 1H-NMR. Consistent with previous studies, the microbiota of children with ASD contained a higher number of Clostridium spp. and a lower number of bifidobacteria compared with non-autistic children. B-GOS administration significantly increased bifidobacterial populations in each compartment of the models, both with autistic and non-autistic-derived samples, and lactobacilli in the final vessel of non-autistic models. In addition, changes in other bacterial population have been seen in particular for Clostridium, Rosburia, Bacteroides, Atopobium, Faecalibacterium prausnitzii, Sutterella spp. and Veillonellaceae. Furthermore, the addition of B-GOS to the models significantly altered short-chain fatty acid production in both groups, and increased ethanol and lactate in autistic children.

PLoS One. 2016 Sep 9;11(9):e0162604. doi: 10.1371/journal.pone.0162604. eCollection 2016.

An In Vitro Approach to Study Effects of Prebiotics and Probiotics on the Faecal Microbiota and Selected Immune Parameters Relevant to the Elderly.

Liu Y, Gibson GR, Walton GE.

Abstract

The aging process leads to alterations of gut microbiota and modifications to the immune response, such changes may be associated with increased disease risk. Prebiotics and probiotics can modulate microbiome changes induced by aging; however, their effects have not been directly compared. The aim of this study was to use anaerobic batch culture fermenters to assess the impact of various fermentable carbohydrates and microorganisms on the gut microbiota and selected immune markers. Elderly volunteers were used as donors for these experiments to enable relevance to an aging population. The impact of fermentation supernatants on immune markers relevant to the elderly were assessed in vitro. Levels of IL-1β, IL-6, IL-8, IL-10 and TNF-α in peripheral blood mononuclear cell culture supernatants were measured using flow cytometry. Trans-galactooligosaccharides (B-GOS) and inulin both stimulated bifidobacteria compared to other treatments ($p<0.05$). Fermentation supernatants taken from faecal batch cultures supplemented with B-GOS, inulin, B. bifidum, L. acidophilus and Ba. coagulans inhibited LPS induced TNF-α ($p<0.05$). IL-10 production, induced by LPS, was enhanced by fermentation supernatants from faecal batch cultures supplemented with B-GOS, inulin, B. bifidum, L. acidophilus, Ba. coagulans and Bac. thetaiotaomicron ($p<0.05$). To conclude, prebiotics and probiotics could lead to potentially beneficial effects to host health by targeting specific bacterial groups, increasing saccharolytic fermentation and decreasing inflammation associated with aging. Compared to probiotics, prebiotics led to greater microbiota modulation at the genus level within the fermenters.

Br J Nutr. 2016 Aug;116(3):480-6. doi: 10.1017/S0007114516002269. Epub 2016 Jun 8.

Fermentation properties and potential prebiotic activity of Bimuno® galacto-oligosaccharide (65 % galacto-oligosaccharide content) on in vitro gut microbiota parameters.

Grimaldi R, Swann JR, Vulevic J, Gibson GR, Costabile A.

Abstract

Prebiotic oligosaccharides have the ability to generate important changes in the gut microbiota composition that may confer health benefits to the host. Reducing the impurities in prebiotic mixtures could expand their applications in food industries and improve their selectivity and prebiotic effect on the potential beneficial bacteria such as bifidobacteria and lactobacilli. This study aimed to determine the in vitro potential fermentation properties of a 65 % galacto-oligosaccharide (GOS) content Bimuno® GOS (B-GOS) on gut microbiota composition and their metabolites. Fermentation of 65 % B-GOS was compared with 52 % B-GOS in pH- and volume-controlled dose-response anaerobic batch culture experiments. In total, three different doses (1, 0·5 and 0·33 g equivalent to 0·1, 0·05 and 0·033 g/l) were tested. Changes in the gut microbiota during a time course were identified by fluorescence in situ hybridisation, whereas small molecular weight metabolomics profiles and SCFA were determined by 1H-NMR analysis and GC, respectively. The 65 % B-GOS showed positive modulation of the microbiota composition during the first 8 h of fermentation with all doses. Administration of the specific doses of B-GOS induced a significant increase in acetate as the major SCFA synthesised compared with propionate and butyrate concentrations, but there were no significant differences between substrates. The 65 % B-GOS in syrup format seems to have, in all the analysis, an efficient prebiotic effect. However, the applicability of such changes remains to be shown in an in vivo trial.

J Nutr. 2013 Mar;143(3):324-31. doi: 10.3945/jn.112.166132. Epub 2013 Jan 9.

A mixture of trans-galactooligosaccharides reduces markers of metabolic syndrome and modulates the fecal microbiota and immune function of overweight adults.

Vulevic J, Juric A, Tzortzis G, Gibson GR.

Abstract

Metabolic syndrome is a set of disorders that increases the risk of developing cardiovascular disease. The gut microbiota is altered toward a less beneficial composition in overweight adults and this change can be accompanied by inflammation. Prebiotics such as galactooligosaccharides can positively modify the gut microbiota and immune system; some may also reduce blood lipids. We assessed the effect of a galactooligosaccharide mixture [Bi2muno (B-GOS)] on markers of metabolic syndrome, gut microbiota, and immune function in 45 overweight adults with ≥3 risk factors associated with metabolic syndrome in a double-blind, randomized, placebo (maltodextrin)-controlled, crossover study (with a 4-wk wash-out period between interventions). Whole blood, saliva, feces, and anthropometric measurements were taken at the beginning, wk 6, and end of each 12-wk intervention period. Predominant groups of fecal bacteria were quantified and full blood count, markers of inflammation and lipid metabolism, insulin, and glucose were measured. B-GOS increased the number of fecal bifidobacteria at the expense of less desirable groups of bacteria. Increases in fecal secretory IgA and decreases in fecal calprotectin, plasma C-reactive protein, insulin, total cholesterol (TC), TG, and the TC:HDL cholesterol ratio were also observed. Administration of B-GOS to overweight adults resulted in positive effects on the composition of the gut microbiota, the immune response, and insulin, TC, and TG concentrations. B-GOS may be a useful candidate for the enhancement of gastrointestinal health, immune function, and the reduction of metabolic syndrome risk factors in overweight adults.

Eur J Clin Nutr. 2010 Feb;64(2):146-52. doi: 10.1038/ejcn.2009.120. Epub 2009 Sep 16.

A double-blind, placebo-controlled, randomized human study assessing the capacity of a novel galacto-oligosaccharide mixture in reducing travellers' diarrhoea.

Drakoularakou A, Tzortzis G, Rastall RA, Gibson GR.

Abstract

BACKGROUND/OBJECTIVES:

Prebiotics have attracted interest for their ability to positively affect the colonic microbiota composition, thus increasing resistance to infection and diarrhoeal disease. This study assessed the effectiveness of a prebiotic galacto-oligosaccharide mixture (B-GOS) on the severity and/or incidence of travellers' diarrhoea (TD) in healthy subjects.

SUBJECTS/METHODS:

The study was a placebo-controlled, randomized, double blind of parallel design in 159 healthy volunteers, who travelled for minimum of 2 weeks to a country of low or high risk for TD. The investigational product was the B-GOS and the placebo was maltodextrin. Volunteers were randomized into groups with an equal probability of receiving either the prebiotic or placebo. The protocol comprised of a 1 week pre-holiday period recording bowel habit, while receiving intervention and the holiday period. Bowel habit included the number of bowel movements and average consistency of the stools as well as occurrence of abdominal discomfort, flatulence, bloating or vomiting. A clinical report was completed in the case of diarrhoeal incidence. A post-study questionnaire was also completed by all subjects on their return.

RESULTS:

Results showed significant differences between the B-GOS and the placebo group in the incidence ($P<0.05$) and duration ($P<0.05$) of TD. Similar findings occurred on abdominal pain ($P<0.05$) and the overall quality of life assessment ($P<0.05$).

CONCLUSIONS:

Consumption of the tested galacto-oligosaccharide mixture showed significant potential in preventing the incidence and symptoms of TD.

Am J Clin Nutr. 2008 Nov;88(5):1438-46.

Modulation of the fecal microflora profile and immune function by a novel trans-galactooligosaccharide mixture (B-GOS) in healthy elderly volunteers.

Vulevic J, Drakoularakou A, Yaqoob P, Tzortzis G, Gibson GR.

Abstract

BACKGROUND:

Aging is associated with reduced numbers of beneficial colonic bifidobacteria and impaired immunity. Galactooligosaccharides (GOSs) stimulate the growth of bifidobacteria in younger adults, but little is known about their effects in the elderly and their immunomodulatory capacity.

OBJECTIVE:

We assessed the effect of a prebiotic GOS mixture (B-GOS) on immune function and fecal microflora composition in healthy elderly subjects.

DESIGN:

In a double-blind, placebo-controlled, crossover study, 44 elderly subjects were randomly assigned to receive either a placebo or the B-GOS treatment (5.5 g/d). Subjects consumed the treatments for 10 wk, and then went through a 4-wk washout period, before switching to the other treatment for the final 10 wk. Blood and fecal samples were collected at the beginning, middle (5 wk), and end of the test period. Predominant bacterial groups were quantified, and phagocytosis, natural killer (NK) cell activity, cytokine production, plasma cholesterol, and HDL cholesterol were measured.

RESULTS:

B-GOS significantly increased the numbers of beneficial bacteria, especially bifidobacteria, at the expense of less beneficial groups compared with the baseline and placebo. Significant increases in phagocytosis, NK cell activity, and the production of antiinflammatory cytokine interleukin-10 (IL-10) and significant reduction in the production of proinflammatory cytokines (IL-6, IL-1beta, and tumor necrosis factor-alpha) were also observed. B-GOS exerted no effects on total cholesterol or HDL-cholesterol production, however.

CONCLUSIONS:

B-GOS administration to healthy elderly persons resulted in positive effects on both the microflora composition and the immune response. Therefore, B-GOS may be a useful dietary candidate for the enhancement of gastrointestinal health and immune function in elderly persons.

Minerva Gastroenterol Dietol. 2013 Dec;59(4):329-40.

Role of PHGG as a dietary fiber: a review article.

Quartarone G.

Abstract

AIM:

Functional and metabolic effects of dietary fiber are recognized by the scientific, clinical and nutritional experts. Dietary fiber plays a very significant role in modifying the intestinal microbiota, exerting prebiotic effects such as stimulating the growth and/or function of beneficial intestinal microorganisms. Changes in the gut microbiota composition are classically considered as one of the many factors involved in the pathogenesis of either inflammatory bowel disease or irritable bowel syndrome. The use of particular food products with a prebiotic effect has thus been tested in clinical trials with the objective to improve the clinical activity and well-being of patients with such disorders. Partially Hydrolyzed Guar Gum (PHGG) is a natural dietary fiber: it is a white powder, water-soluble, colorless and transparent in water solution and almost tasteless. PHGG is stable and soluble at various pH levels commonly found in foods as well as resistant to heat, acid, salt, high pressure and digestive enzymes. Low viscosity of PHGG provides a distinct advantage for the use of fiber in enteral feeding products to be administered through feeding tubes. It has been studied in adults, both healthy volunteers and patients, in different disorders such as constipation, irritable bowel syndrome (IBS), enteral nutrition, small intestine bacterial overgrowth (SIBO) and, very recently, in children suffering from functional abdominal pain according to the Rome III Criteria definition for functional gastrointestinal disorders (FGIDs). This review takes stock of the situation concerning what is known to date on PHGG as dietary fiber, in order to give the health care professionals, such as gastroenterologists, dieticians and general practitioners, a complete overview on its intrinsic characteristics, preclinical and clinical evaluations, uses in different situations as supportive therapy in the management of the main intestinal functional disorders both in adults and in children.

METHODS:

All the papers on PHGG, published from the early 1990s of the Last Century to the Year 2013, have been considered. All types of publications have been included. PubMed, Medline, Ovid were the main sources adopted for data retrieving.

RESULTS:

PHGG has been studied in both animals and humans; its safety is well known and several clinical uses are well established. Concerning the modulation of metabolism in human, very little has been done to date and the studies have been focused, for the most part, on the functional diseases: PHGG has been proved to be useful in treating both IBS -C and D symptoms, not only in adults but also in children; data on constipation are relatively scarce and what can be deduced from the Literature is that the high concentration of fiber gives the PHGG the possibility of being used effectively in acceptable dosages (up to 22 g/day) even in situations such as chronic constipation. The use in clinical nutrition has revealed the flexibility of the compound which, owing to its peculiar characteristics, does not gel and remains liquid, PHGG can be used successfully in patients in enteral nutrition lowering the incidence of diarrhea. New open horizons can be glimpsed for SIBO treatment, lowering or maximizing the antibiotics use.

CONCLUSION:

Not all the fibers are the same: this is a fact. Promoting the specific knowledge of their characteristics is very important if healthcare professionals want to give their patients the best options for functional gastrointestinal disorders or nutritional needs. PHGG has been proved to be safe and effective in promoting gut health.

Nutrition. 2006 Mar;22(3):334-42.

Role of partially hydrolyzed guar gum in the treatment of irritable bowel syndrome.

Giannini EG, Mansi C, Dulbecco P, Savarino V.

Abstract

Irritable bowel syndrome (IBS) is the world's most common gastrointestinal functional disorder and is associated with several social and economic costs. Health-related quality of life is often impaired in patients with IBS. The pathophysiologic mechanisms underlying IBS remain poorly defined. The therapeutic approach to patients with IBS is based on symptoms, and fibers may play an important role in treatment. Among the various types of fiber, water-soluble, non-gelling fibers seem to be a promising option for treatment of IBS. Partially hydrolyzed guar gum (PHGG) is a water-soluble, non-gelling fiber that has provided therapeutic benefits. In clinical trials, PHGG decreased symptoms in constipation-predominant and diarrhea-predominant forms of IBS and decreased abdominal pain. Further, an improvement in quality of life was observed in patients with IBS during and after treatment with PHGG. Moreover, PHGG seems to have prebiotic properties because it increases the colonic contents of short-chain fatty acids, Lactobacilli, and Bifidobacteria.

Anaerobe. 2016 Dec;42:60-66.

In vitro analysis of partially hydrolyzed guar gum fermentation on identified gut microbiota.

Carlson J, Gould T, Slavin J.

Abstract

BACKGROUND:

Prebiotic dietary fibers resist digestion in the upper gastrointestinal tract and allow for stimulation of bacteria in the distal intestine and colon. Stimulation of bacteria among different individuals varies greatly, depending on a wide range of variables.

OBJECTIVE:

To determine the range of differences in response between individuals, a preclinical in vitro fermentation was conducted with six fecal donors. The primary objective was to compare the fecal microbiota of six individuals at baseline, 12 h and 24 h post-exposure to partially hydrolyzed guar gum (PHGG).

METHOD:

Fecal donations were collected from six healthy individuals consuming a non-specific Western diet, free of antibiotic treatments in the past year, not affected by any GI diseases and not consuming any probiotic or prebiotic supplements. Fecal samples were exposed to 0.5 g of PHGG and measured for bacterial changes at 0, 12 and 24 h based on 16S rRNA sequencing.

RESULTS:

Parabacteroides increased from 3.48% of sequence reads to 10.62% of sequence reads after 24 h ($p = 0.0181$) and Bacteroidetes increased from 45.89% of sequence reads to 50.29% of sequence reads ($p = 0.0008$).

CONCLUSIONS:

PHGG stimulates growth of Parabacteroides, a genus of bacteria that have been inversely associated with IBS and ulcerative colitis. PHGG provides stimulation of beneficial Bacteroidetes (Bacteroides and Parabacteroides), which may be correlated with many positive health markers and outcomes. PHGG is a prebiotic dietary fiber that is readily fermentable.

Br J Nutr. 2016 Oct;116(7):1199-1205.

Partially hydrolysed guar gum ameliorates murine intestinal inflammation in association with modulating luminal microbiota and SCFA.

Takagi T, Naito Y, Higashimura Y, Ushiroda C, Mizushima K, Ohashi Y, Yasukawa Z, Ozeki M, Tokunaga M, Okubo T, Katada K, Kamada K, Uchiyama K, Handa O, Itoh Y, Yoshikawa T.

Abstract

Partially hydrolysed guar gum (PHGG), a water-soluble dietary fibre produced by the controlled partial enzymatic hydrolysis of guar gum beans, has various physiological roles. This study aimed to elucidate the beneficial effects of PHGG on colonic mucosal damage in a murine 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis model. Acute colitis was induced in male C57BL/6 mice with TNBS after 2 weeks of pre-feeding with PHGG (5 %). The colonic mucosal inflammation was evaluated using macroscopic damage scores, and neutrophil infiltration was assessed by measuring tissue-associated myeloperoxidase (MPO) activity in the colonic mucosa. TNF-α expression in the colonic mucosa was measured by ELISA and real-time PCR. Moreover, the intestinal microbiota and production of SCFA were assessed by real-time PCR and HPLC, respectively. Colonic damage due to TNBS administration was significantly ameliorated by PHGG treatment. Furthermore, PHGG significantly inhibited increases in MPO activity and TNF-α protein and mRNA expression in the colonic mucosa in TNBS-induced colitis. On analysis of intestinal microbiota, we found that the concentration of the Clostridium coccoides group (Clostridium cluster XIVa), the Clostridium leptum subgroup (Clostridium cluster IV) and the Bacteroides fragilis group had significantly increased in PHGG-fed mice. On analysis of SCFA, we found that the caecal content of acetic acid, propionic acid and butyric acid had significantly increased in PHGG-fed mice. Together, these results suggest that chronic ingestion of PHGG prevents the development of TNBS-induced colitis in mice by modulating the intestinal microbiota and SCFA, which may be significant in the development of therapeutics for inflammatory bowel disease.

J Pediatr Gastroenterol Nutr. 2016 Jul;63 Suppl 1:S25-6.

Probiotics for Irritable Bowel Syndrome: Clinical Data in Children.

Giannetti E, Staiano A.

Abstract

PURPOSE OF REVIEW:

The purpose of this review was to summarize the evidence regarding probiotics treatment for pediatric IBS.

RECENT FINDINGS:

The overall management of children with IBS should be tailored to the patient's specific symptoms and identifiable triggers. The four major therapeutic approaches include: pharmacologic, dietary, psychosocial, and complementary/alternative medicine interventions. Although there is limited evidence for efficacy of pharmacological therapies such as antispasmodics and anti-diarrheals, these may have a role in severe cases. A Cochrane review concluded that only weak evidence exists regarding beneficial effects of pharmacological agents in providing relief from symptoms in functional abdominal pain (AP) in children. Role of antibiotics in treatment of children with IBS remains controversial. Various non-pharmacologic treatments are available for pediatric IBS. In a recent systematic review including 24 studies some evidence was found indicating beneficial effects of partially hydrolyzed guar gum (PHGG), cognitive behavioral therapy, hypnotherapy, and probiotics (LGG and VSL#3).Few randomized clinical trials (RCTs) are available in children. A meta-analysis including 9 trials which tested different probiotics as a treatment for Functional Gastrointestinal Disorders (FGIDs) in children and adolescents concluded that Lactobacillus GG, Lactobacillus reuteri DSM 17938 and VSL#3 significantly increased treatment success. We recently showed that, in children with IBS, a mixture of Bifidobacterium infantis M-63®, breve M-16V® and longum BB536® is safe and is associated with better AP control and improved quality of life when compared to placebo.

SUMMARY:

Probiotics are emerging as new therapeutic tools in FGIDs, due to the recognition of the importance of gut microbiota in influencing brain-gut interactions, and of the role played by intestinal infections in the genesis of AP-FGIDs. Preclinical data suggest that changes in the gut microbiota can affect brain signaling systems related to pain and associated emotional behavior. Therefore, probiotics could play a relevant role in the management of FGIDs, by affecting the gut microbiota or by altering brain function and pain perception centrally.

Benef Microbes. 2015;6(4):451-5. doi: 10.3920/BM2014.0118. Epub 2015 Feb 12.

Consumption of partially hydrolysed guar gum stimulates Bifidobacteria and butyrate-producing bacteria in the human large intestine.

Ohashi Y, Sumitani K, Tokunaga M, Ishihara N, Okubo T, Fujisawa T.

Abstract

Partially hydrolysed guar gum (PHGG) is a water-soluble dietary fibre that is non-digestible in the upper gastrointestinal tract. It is believed that PHGG benefits the health of hosts by altering the colonic microbiota and stimulating short-chain fatty acid (SCFA) production. However, it remains unclear which bacteria ferment PHGG in the human large intestine. In this study, the effect of PHGG on faecal bacteria was analysed to specify the bacteria that contribute to the fermentation of PHGG in the human large intestine. Ten healthy volunteers consumed PHGG (6 g/day) for 2 weeks. Faeces were collected at 2 weeks prior to consumption, at the end of 2 weeks of consumption, and 2 weeks after consumption of PHGG. Bacterial DNA was extracted from these collected faeces and subjected to real-time PCR using bacterial group- or species-specific primers. The copy number of the butyryl-CoA CoA-transferase gene and the 16S rRNA gene copy numbers of Bifidobacterium, the Clostridium coccoides group, the Roseburia/ Eubacterium rectale group, Eubacterium hallii, and butyrate-producing bacterium strain SS2/1 were significantly increased by the intake of PHGG. Other bacteria and bacterial groups were not significantly influenced by the intake of PHGG. It was believed that the Roseburia/E. rectale group bacteria, Bifidobacterium, the lactate-utilising, butyrate-producing bacteria, E. hallii and bacterium strain SS2/1, would contribute to the fermentation of PHGG in the human large intestine. PHGG may benefit health by stimulating Bifidobacterium and butyrate-producing bacteria in the human large intestine.

Nutr Hosp. 2012 Jan-Feb;27(1):123-9. doi: 10.1590/S0212-16112012000100014.

Microbiota benefits after inulin and partially hydrolized guar gum supplementation: a randomized clinical trial in constipated women.

Linetzky Waitzberg D, Alves Pereira CC, Logullo L, Manzoni Jacintho T, Almeida D, Teixeira da Silva ML, Matos de Miranda Torrinhas RS.

Abstract

INTRODUCTION:

Prebiotics positively affect gut microbiota composition, thus improving gut function. These properties may be useful for the treatment of constipation.

OBJECTIVES:

This study assessed the tolerance and effectiveness of a prebiotic inulin/partially hydrolyzed guar gum mixture (I-PHGG) for the treatment of constipation in females, as well as its influence on the composition of intestinal microbiota and production of short chain fatty acids.

METHODS:

Our study enrolled 60 constipated female health worker volunteers. Participants reported less than 3 bowel movements per week. Volunteers were randomized to treatment with prebiotic or placebo. Treatment consisted of 3 weeks supplementation with 15 g/d IPHGG (fiber group) or maltodextrin (placebo group). Abdominal discomfort, flatulence, stool consistency, and bowel movements were evaluated by a recorded daily questionnaire and a weekly interview. Changes in fecal bacterial population and short chain fatty acids were assessed by real-time PCR and gas chromatography, respectively.

RESULTS:

There was an increased frequency of weekly bowel movements and patient satisfaction in both the fiber and placebo groups with no significant differences. Total Clostridium sp significantly decreased in the fiber group ($p = 0.046$) and increased in the placebo group ($p = 0.047$). There were no changes in fecal short chain fatty acid profile.

CONCLUSIONS:

Consumption of I-PHGG produced clinical results comparable to placebo in constipated females, but had additional protective effects on gut microbiota by decreasing the amount of pathological bacteria of the Clostridium genera.

Nutr Metab (Lond). 2016 Feb 6;13:10.

Randomized clinical study: Partially hydrolyzed guar gum (PHGG) versus placebo in the treatment of patients with irritable bowel syndrome.

Niv E, Halak A, Tiommny E, Yanai H, Strul H, Naftali T, Vaisman N.

Abstract

BACKGROUND:

The treatment of Irritable bowel syndrome (IBS) is still challenging. Partially hydrolyzed guar gum (PHGG) is a known prebiotic fiber. To assess the effects of PHGG on clinical symptoms of IBS patients in a prospective randomized double blind placebo-controlled study.

METHODS:

Suitable IBS patients were recruited into an 18-week-long study (2 weeks of run-in, 12 weeks of treatment and 4 weeks of follow-up). They were blindly randomized to receive 6 gr of PHGG or placebo. Treatment efficacy was evaluated by the Francis Severity IBS score, the IBS quality-of-life scores and scored parameters of weekly journal of symptoms. Deltas of changes between the final and baseline scores were compared between two groups.

RESULTS:

Of 121 patients who underwent randomization, 108 patients (49 in the PHGG group and 59 in the placebo group) had all the data needed for intention-to-treat analysis. A 12-week administration of PHGG led to a significant improvement of journal bloating score in the PHGG group versus placebo (-4.1±13.4 versus -1.2±11.9, P=0.03), as well as in bloating+gasses score (-4.3±10.4 versus -1.12±10.5, P = 0.035). The effect lasted for at least 4 weeks after the last PHGG administration. PHGG had no effect on other journal reported IBS symptoms or on Severity and Quality of life scores. There were no significant side effects associated with PHGG ingestion. The rate of dropouts was significantly higher among patients in the placebo group compared with the PHGG group (49.15% versus 22.45%, respectively, P = 0.01).

CONCLUSIONS:

The results of this study support the administration of 6 g/day PHGG for IBS patients with bloating.

Phyto-Biotic Blend – Selected Background Documents

Biol Pharm Bull. 2017;40(6):902-909. doi: 10.1248/bpb.b17-00141.

Anti-stress Effect of Green Tea with Lowered Caffeine on Humans: A Pilot Study.

Unno K, Yamada H, Iguchi K, Ishida H, Iwao Y, Morita A, Nakamura Y.

Abstract

Theanine, an amino acid in tea, has significant anti-stress effects on animals and humans. However, the effect of theanine was blocked by caffeine and gallate-type catechins, which are the main components in tea. We examined the anti-stress effect of green tea with lowered caffeine, low-caffeine green tea, on humans. The study design was a single-blind group comparison and participants (n=20) were randomly assigned to low-caffeine or placebo tea groups. These teas (≥500 mL/d), which were eluted with room temperature water, were taken from 1 week prior to pharmacy practice and continued for 10 d in the practice period. The participants ingested theanine (ca. 15 mg/d) in low-caffeine green tea. To assess the anxiety of participants, the state-trait anxiety inventory test was used before pharmacy practice. The subjective stress of students was significantly lower in the low-caffeine-group than in the placebo-group during pharmacy practice. The level of salivary α-amylase activity, a stress marker, increased significantly after daily pharmacy practice in the placebo-group but not in the low-caffeine-group. These results suggested that the ingestion of low-caffeine green tea suppressed the excessive stress response of students.

Pharmacol Biochem Behav. 2013 Oct;111:128-35.

Anti-stress effect of theanine on students during pharmacy practice: positive correlation among salivary α-amylase activity, trait anxiety and subjective stress.

Unno K, Tanida N, Ishii N, Yamamoto H, Iguchi K, Hoshino M, Takeda A, Ozawa H, Ohkubo T, Juneja LR, Yamada H.

Abstract

PURPOSE:

Theanine, an amino acid in tea, has significant anti-stress effect on experimental animals under psychosocial stress. Anti-stress effect of theanine on humans was evaluated in 5th-year university students during pharmacy practice.

METHOD:

The study design was a single-blind group comparison and participants (n=20) were randomly assigned to theanine or placebo groups. Theanine or placebo (lactose) tablets (200 mg, twice a day, after breakfast and lunch) were taken from 1 week prior to the pharmacy practice and continued for 10 days in the practice period. To assess the anxiety of the participants, the state-trait anxiety inventory test was carried out before the pharmacy practice. Salivary α-amylase activity (sAA) was measured as a marker of sympathetic nervous system activity.

RESULTS:

In the placebo-group, sAA in the morning (pre-practice sAA) was higher than in theanine-group during the pharmacy practice (p=0.032). Subjective stress was significantly lower in the theanine-group than in the placebo-group (p=0.020). These results suggest that theanine intake had anti-stress effect on students. Furthermore, students with higher pre-practice sAA showed significantly higher trait anxiety in both groups (p=0.015). Similarly, higher pre-practice sAA was correlated to shorter sleeping time in both groups (p=0.41×10(-3)).

CONCLUSION:

Stressful condition increased the level of sAA that was essentially affected by individual trait anxiety. The low levels of pre-practice sAA and subjective stress in the theanine-group suggest that theanine intake suppressed initial stress response of students assigned for a long-term commitment of pharmacy practice.

Nutrients. 2016 Jan 19;8(1). pii: E53. doi: 10.3390/nu8010053.

Anti-Stress, Behavioural and Magnetoencephalography Effects of an L-Theanine-Based Nutrient Drink: A Randomised, Double-Blind, Placebo-Controlled, Crossover Trial.

White DJ, de Klerk S, Woods W, Gondalia S, Noonan C, Scholey AB.

Abstract

L-theanine (γ-glutamylethylamide) is an amino acid found primarily in the green tea plant. This study explored the effects of an L-theanine-based nutrient drink on mood responses to a cognitive stressor. Additional measures included an assessment of cognitive performance and resting state alpha oscillatory activity using magnetoencephalography (MEG). Thirty-four healthy adults aged 18-40 participated in this double-blind, placebo-controlled, balanced crossover study. The primary outcome measure, subjective stress response to a multitasking cognitive stressor, was significantly reduced one hour after administration of the L-theanine drink when compared to placebo. The salivary cortisol response to the stressor was reduced three hours post-dose following active treatment. No treatment-related cognitive performance changes were observed. Resting state alpha oscillatory activity was significantly greater in posterior MEG sensors after active treatment compared to placebo two hours post-dose; however, this effect was only apparent for those higher in trait anxiety. This change in resting state alpha oscillatory activity was not correlated with the change in subjective stress response or the cortisol response, suggesting further research is required to assess the functional relevance of these treatment-related changes in resting alpha activity. These findings further support the anti-stress effects of L-theanine.

Crit Rev Food Sci Nutr. 2017 May 24;57(8):1681-1687.

L-theanine, unique amino acid of tea, and its metabolism, health effects, and safety.

Türközü D, Şanlier N.

Abstract

Tea has been a very popular beverage around the world for centuries. The reason that it is delicious, enabling hydration, showing warming and relaxing effect can be mentioned why it is consumed so much in addition to its prominent health effects. Although the catechins and caffeine are the primary bioactive components that are related with the health effects of the tea, the health effects of theanine amino acid, which is a nonproteinic amino acid special to tea, has become prominent in recent years. It has been known that the theanine amino acid in tea has positive effects especially on relaxing, cognitive performance, emotional status, sleep quality, cancer, cardiovascular diseases, obesity, and common cold. The results of acute and chronic toxicity tests conducted on the safety of theanine express that L-theanine is reliable in general even if it is consumed too much with diet. However, it has not revealed a clear evidence-based result yet regarding theanine metabolism, health effects, and its safety. Within this frame, chemical structure of theanine, its biosynthesis, dietary sources, metabolism, health effects, and safety are discussed in present study.

Scientific World Journal. 2014;2014:419032

Effects of L-theanine on posttraumatic stress disorder induced changes in rat brain gene expression.

Ceremuga TE, Martinson S, Washington J, Revels R, Wojcicki J, Crawford D, Edwards R, Kemper JL, Townsend WL, Herron GM, Ceremuga GA, Padron G, Bentley M.

Abstract

Posttraumatic stress disorder (PTSD) is characterized by the occurrence of a traumatic event that is beyond the normal range of human experience. The future of PTSD treatment may specifically target the molecular mechanisms of PTSD. In the US, approximately 20% of adults report taking herbal products to treat medical illnesses. L-theanine is the amino acid in green tea primarily responsible for relaxation effects. No studies have evaluated the potential therapeutic properties of herbal medications on gene expression in PTSD. We evaluated gene expression in PTSD-induced changes in the amygdala and hippocampus of Sprague-Dawley rats. The rats were assigned to PTSD-stressed and nonstressed groups that received either saline, midazolam, L-theanine, or L-theanine + midazolam. Amygdala and hippocampus tissue samples were analyzed for changes in gene expression. One-way ANOVA was used to detect significant difference between groups in the amygdala and hippocampus. Of 88 genes examined, 17 had a large effect size greater than 0.138. Of these, 3 genes in the hippocampus and 5 genes in the amygdala were considered significant ($P < 0.05$) between the groups. RT-PCR analysis revealed significant changes between groups in several genes implicated in a variety of disorders ranging from PTSD, anxiety, mood disorders, and substance dependence.

Nutr Neurosci. 2014 Nov;17(6):279-83.

Advantageous effect of theanine intake on cognition.

Tamano H, Fukura K, Suzuki M, Sakamoto K, Yokogoshi H, Takeda A.

Abstract

Theanine, γ-glutamylethylamide, is one of the major amino acid components in green tea. On the basis of the preventive effect of theanine intake after weaning on stress-induced impairment of recognition memory, the advantageous effect of theanine intake on recognition memory was examined in young rats, which were fed water containing 0.3% theanine for 3 weeks after weaning. The rats were subjected to object recognition test. Object recognition memory was maintained in theanine-administered rats 48 hours after the training, but not in the control rats. When in vivo dentate gyrus long-term potentiation (LTP) was induced, it was more greatly induced in theanine-administered rats than in the control rats. The levels of brain-derived neurotropic factor and nerve growth factor in the hippocampus were significantly higher in theanine-administered rats than in the control rats. The present study indicates the advantageous effect of theanine intake after weaning on recognition memory. It is likely that theanine intake is of advantage to the development of hippocampal function after weaning.

Brain Res Bull. 2013 Jun;95:1-6.

Preventive effect of theanine intake on stress-induced impairments of hippocamapal long-term potentiation and recognition memory.

Tamano H, Fukura K, Suzuki M, Sakamoto K, Yokogoshi H, Takeda A.

Abstract

Theanine, γ-glutamylethylamide, is one of the major amino acid components in green tea. On the basis of the preventive effect of theanine intake after birth on mild stress-induced attenuation of hippocamapal CA1 long-term potentiation (LTP), the present study evaluated the effect of theanine intake after weaning on stress-induced impairments of LTP and recognition memory. Young rats were fed water containing 0.3% theanine for 3 weeks after weaning and subjected to water immersion stress for 30min, which was more severe than tail suspension stress for 30s used previously. Serum corticosterone levels were lower in theanine-administered rats than in the control rats even after exposure to stress. CA1 LTP induced by a 100-Hz tetanus for 1s was inhibited in the presence of 2-amino-5-phosphonovalerate (APV), an N-methyl-d-aspartate (NMDA) receptor antagonist, in hippocampal slices from the control rats and was attenuated by water immersion stress. In contrast, CA1 LTP was not significantly inhibited in the presence of APV in hippocampal slices from theanine-administered rats and was not attenuated by the stress. Furthermore, object recognition memory was impaired in the control rats, but not in theanine-administered rats. The present study indicates the preventive effect of theanine intake after weaning on stress-induced impairments of hippocampal LTP and recognition memory. It is likely that the modification of corticosterone secretion after theanine intake is involved in the preventive effect.

Brain Res. 2013 Mar 29;1503:24-32.

Protective effect of l-theanine on chronic restraint stress-induced cognitive impairments in mice.

Tian X, Sun L, Gou L, Ling X, Feng Y, Wang L, Yin X, Liu Y.

Abstract

The present work was aimed to study the protective effect of l-theanine on chronic restraint stress (CRS)-induced cognitive impairments in mice. The stress was produced by restraining the animals in well-ventilated polypropylene tubes (3.2 cm in diameter ×10.5 cm in length) for 8h once daily for 21 consecutive days. L-theanine (2 and 4 mg/kg) was administered 30 min before the animals subjected to acute immobilized stress. At week 4, mice were subjected to Morris water maze and step-through tests to measure the cognitive function followed by oxidative parameters and corticosterone as well as catecholamines (norepinephrine and dopamine) subsequently. Our results showed that the cognitive performances in CRS group were markedly deteriorated, accompanied by noticeable alterations in oxidative parameters and catecholamine levels in the hippocampus and the cerebral cortex as well as corticosterone and catecholamine levels in the serum. However, not only did l-theanine treatment exhibit a reversal of the cognitive impairments and oxidative damage induced by CRS, but also reversed the abnormal level of corticosterone in the serum as well as the abnormal levels of catecholamines in the brain and the serum. This study indicated the protective effect of l-theanine against CRS-induced cognitive impairments in mice.

J Physiol Anthropol. 2012 Oct 29;31:28.

Effects of L-theanine or caffeine intake on changes in blood pressure under physical and psychological stresses.

Yoto A, Motoki M, Murao S, Yokogoshi H.

Abstract

BACKGROUND:

L-theanine, an amino acid contained in green tea leaves, is known to block the binding of L-glutamic acid to glutamate receptors in the brain, and has been considered to cause anti-stress effects by inhibiting cortical neuron excitation. Both L-theanine and caffeine, which green tea contains, have been highlighted for their beneficial effects on cognition and mood.

METHODS:

In this study, we investigated the effects of orally administered L-theanine or caffeine on mental task performance and physiological activities under conditions of physical or psychological stress in humans. Fourteen participants each underwent three separate trials, in which they orally took either L-theanine + placebo, caffeine + placebo, or placebo only.

RESULTS:

The results after the mental tasks showed that L-theanine significantly inhibited the blood-pressure increases in a high-response group, which consisted of participants whose blood pressure increased more than average by a performance of a mental task after placebo intake. Caffeine tended to have a similar but smaller inhibition of the blood-pressure increases caused by the mental tasks. The result of the Profile of Mood States after the mental tasks also showed that L-theanine reduced the Tension-Anxiety scores as compared with placebo intake.

CONCLUSIONS:

The findings above denote that L-theanine not only reduces anxiety but also attenuates the blood-pressure increase in high-stress-response adults.

Exp Physiol. 2013 Jan;98(1):290-303.

Ingestion of theanine, an amino acid in tea, suppresses psychosocial stress in mice.

Unno K, Iguchi K, Tanida N, Fujitani K, Takamori N, Yamamoto H, Ishii N, Nagano H, Nagashima T, Hara A, Shimoi K, Hoshino M.

Abstract

The antistress effect of theanine (γ-glutamylethylamide), an amino acid in tea, was investigated using mice that were psychosocially stressed from a conflict among male mice in conditions of confrontational housing. Two male mice were housed in the same cage separated by a partition to establish a territorial imperative. When the partition was removed, the mice were co-housed confrontationally. As a marker for the stress response, changes in the adrenal gland were studied in comparison to group-housed control mice (six mice in a cage). Significant adrenal hypertrophy was observed in mice during confrontational housing, which was developed within 24 h and persisted for at least 1 week. The size of cells in the zona fasciculata of the adrenal gland, from which glucocorticoid is mainly secreted, increased (?1.11-fold) in mice during confrontational housing, which was accompanied by a flattened diurnal rhythm of corticosterone and ACTH in blood. The ingestion of theanine (>5 μg ml(-1)) prior to confrontational housing significantly suppressed adrenal hypertrophy. An antidepressant, paroxetin, suppressed adrenal hypertrophy in a similar manner in mice during confrontational housing. In mice that ingested theanine, behavioural depression was also suppressed, and a diurnal rhythm of corticosterone and ACTH was observed, even in mice that were undergoing confrontational housing. Furthermore, the daily dose of theanine (40 μg ml(-1)) blocked the counteracting effects of caffeine (30 μg ml(-1)) and catechin (200 μg ml(-1)). The present study demonstrated that theanine prevents and relieves psychosocial stress through the modulation of hypothalamic-pituitary-adrenal axis activity.

Free Radic Res. 2011 Aug;45(8):966-74.

Theanine intake improves the shortened lifespan, cognitive dysfunction and behavioural depression that are induced by chronic psychosocial stress in mice.

Unno K, Fujitani K, Takamori N, Takabayashi F, Maeda K, Miyazaki H, Tanida N, Iguchi K, Shimoi K, Hoshino M.

Abstract

To evaluate the psychosocial effect on lifespan and cognitive function, this study investigated the effect of confrontational housing on mice because conflict among male mice is a psychosocial stress. In addition, it investigated the anti-stress effect of theanine (γ-glutamylethylamide), an amino acid in tea. Mice were housed under confrontation. That is, two male mice were separately housed in the same cage with a partition for establishing the territorial imperative in each mouse. Then, the partition was removed and mice were co-housed confrontationally (confront-housing) using a model mouse of accelerated-senescence (SAMP10) that exhibited cerebral atrophy and cognitive dysfunction with ageing. It was found that mice began to die earlier under confront-housing than group-housed control mice. Additionally, it was found that cerebral atrophy, learning impairment and behavioural depression were higher in mice under the stressed condition of confront-housing than age-matched mice under group-housing. Furthermore, the level of oxidative damage in cerebral DNA was higher in mice housed confrontationally than group-housed control mice. On the other hand, the consumption of purified theanine (20 μg/ml, 5-6 mg/kg) suppressed the shortened lifespan, cerebral atrophy, learning impairment, behavioural depression and oxidative damage in cerebral DNA. These results suggest that psychosocial stress accelerates age-related alterations such as oxidative damage, lifespan, cognitive dysfunction and behavioural depression. The intake of theanine might be a potential candidate for suppression of disadvantage under psychosocial stress.

Phytother Res. 2011 Nov;25(11):1636-9.

Antidepressant-like effects of L-theanine in the forced swim and tail suspension tests in mice.

Yin C, Gou L, Liu Y, Yin X, Zhang L, Jia G, Zhuang X.

Abstract

L-theanine (γ-glutamylethylamide), an amino acid component of green tea, has been shown to reduce mental and physical stress, and to improve memory function. In this study, the antidepressant effect of L-theanine was investigated in mice using the forced swim test, tail suspension test, open-field test and reserpine test. L-theanine produced an antidepressant-like effect, since the administration of L-theanine at doses of 1, 4 and 20 mg/kg for 10 successive days significantly reduced the immobility time in both the forced swim test and tail suspension test, compared with the control group, without accompanying changes in ambulation in the open-field test. Moreover, L-theanine significantly antagonized reserpine-induced ptosis and hypothermia. Taken together, these results indicate that L-theanine possessed an antidepressant-like effect in mice, which may be mediated by the central monoaminergic neurotransmitter system.

Free Radic Biol Med. 2009 Dec 1;47(11):1601-10.

l-Theanine, an amino acid in green tea, attenuates beta-amyloid-induced cognitive dysfunction and neurotoxicity: reduction in oxidative damage and inactivation of ERK/p38 kinase and NF-kappaB pathways.

Kim TI, Lee YK, Park SG, Choi IS, Ban JO, Park HK, Nam SY, Yun YW, Han SB, Oh KW, Hong JT.

Abstract

Amyloid beta (Abeta)-induced neurotoxicity is a major pathological mechanism of Alzheimer disease (AD). In this study, we investigated the inhibitory effect of l-theanine, a component of green tea (Camellia sinensis), on Abeta(1-42)-induced neuronal cell death and memory impairment. Oral treatment of l-theanine (2 and 4 mg/kg) for 5 weeks in the drinking water of mice, followed by injection of Abeta(1-42) (2 microg/mouse, icv), significantly attenuated Abeta(1-42)-induced memory impairment. Furthermore, l-theanine reduced Abeta(1-42) levels and the accompanying Abeta(1-42)-induced neuronal cell death in the cortex and hippocampus of the brain. Moreover, l-theanine inhibited Abeta(1-42)-induced extracellular signal-regulated kinase (ERK) and p38 mitogen-activated protein kinase as well as the activity of nuclear factor kappaB (NF-kappaB). l-Theanine also significantly reduced oxidative protein and lipid damage and the elevation of glutathione levels in the brain. These data suggest that the positive effects of l-theanine on memory may be mediated by suppression of ERK/p38 and NF-kappaB as well as the reduction of macromolecular oxidative damage. Thus, l-theanine may be useful in the prevention and treatment of AD.

Neurotoxicology. 2008 Jul;29(4):656-62.

Protective effect of the green tea component, L-theanine on environmental toxins-induced neuronal cell death.

Cho HS, Kim S, Lee SY, Park JA, Kim SJ, Chun HS.

Abstract

Several environmental neurotoxins and oxidative stress inducers are known to damage the nervous system and are considered major factors associated with the selective vulnerability of nigral dopaminergic neurons in Parkinson's disease (PD). Gamma-glutamylethylamide (L-theanine), a natural glutamate analog in green tea, has been shown to exert strong anti-ischemic effect. In this study, we investigated the protective effects of L-theanine on neurotoxicity induced by PD-related neurotoxicants, rotenone and dieldrin in cultured human dopaminergic cell line, SH-SY5Y. Our initial experiments revealed that L-theanine (500 microM) attenuated both rotenone- and dieldrin-induced DNA fragmentation and apoptotic death in SH-SY5Y cells. In addition, L-theanine partially prevented both rotenone- and dieldrin-induced heme oxygenase-1 (HO-1) up-regulation. Both rotenone- and dieldrin-induced down-regulation of extracellular signal-regulated kinase1/2 (ERK1/2) phosphorylation was significantly blocked by pretreatment with L-theanine. Furthermore, pretreatment with L-theanine significantly attenuated the down-regulation of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF) production in SH-SY5Y cells. These results suggest that L-theanine directly provide neuroprotection against PD-related neurotoxicants and may be clinically useful for preventing PD symptoms.

Biol Psychol. 2007 Jan;74(1):39-45.

L-Theanine reduces psychological and physiological stress responses.

Kimura K, Ozeki M, Juneja LR, Ohira H.

Abstract

L-Theanine is an amino acid contained in green tea leaves which is known to block the binding of L-glutamic acid to glutamate receptors in the brain. Because the characteristics of L-Theanine suggest that it may influence psychological and physiological states under stress, the present study examined these possible effects in a laboratory setting using a mental arithmetic task as an acute stressor. Twelve participants underwent four separate trials: one in which they took L-Theanine at the start of an experimental procedure, one in which they took L-Theanine midway, and two control trials in which they either took a placebo or nothing. The experimental sessions were performed by double-blind, and the order of them was counterbalanced. The results showed that L-Theanine intake resulted in a reduction in the heart rate (HR) and salivary immunoglobulin A (s-IgA) responses to an acute stress task relative to the placebo control condition. Moreover, analyses of heart rate variability indicated that the reductions in HR and s-IgA were likely attributable to an attenuation of sympathetic nervous activation. Thus, it was suggested that the oral intake of L-Theanine could cause anti-stress effects via the inhibition of cortical neuron excitation.

Nutrition. 2007 May;23(5):419-23.

Effects of Applephenon and ascorbic acid on physical fatigue.

Ataka S, Tanaka M, Nozaki S, Mizuma H, Mizuno K, Tahara T, Sugino T, Shirai T, Kajimoto Y, Kuratsune H, Kajimoto O, Watanabe Y.

Abstract

OBJECTIVE:

We examined the effects of Applephenon and ascorbic acid administration on physical fatigue.

METHODS:

In a double-blinded, placebo-controlled, three-way crossover design, 18 healthy volunteers were randomized to oral Applephenon (1200 mg/d), ascorbic acid (1000 mg/d), or placebo for 8 d. The fatigue-inducing physical task consisted of workload trials on a bicycle ergometer at fixed workloads for 2 h on two occasions. During the test, subjects performed non-workload trials with maximum velocity for 10 s at 30 min (30-min trial) after the start of the test and 30 min before the end of the test (210-min trial).

RESULTS:

The change in maximum velocity between the 30- and 210-min trials was higher in the group given Applephenon than in the group given placebo; ascorbic acid had no effect.

CONCLUSION:

These results suggest that Applephenon attenuates physical fatigue, whereas ascorbic acid does not.

Nutrients. 2015 May 26;7(6):3959-98.

Apples and cardiovascular health--is the gut microbiota a core consideration?

Koutsos A, Tuohy KM, Lovegrove JA.

Abstract

There is now considerable scientific evidence that a diet rich in fruits and vegetables can improve human health and protect against chronic diseases. However, it is not clear whether different fruits and vegetables have distinct beneficial effects. Apples are among the most frequently consumed fruits and a rich source of polyphenols and fiber. A major proportion of the bioactive components in apples, including the high molecular weight polyphenols, escape absorption in the upper gastrointestinal tract and reach the large intestine relatively intact. There, they can be converted by the colonic microbiota to bioavailable and biologically active compounds with systemic effects, in addition to modulating microbial composition. Epidemiological studies have identified associations between frequent apple consumption and reduced risk of chronic diseases such as cardiovascular disease. Human and animal intervention studies demonstrate beneficial effects on lipid metabolism, vascular function and inflammation but only a few studies have attempted to link these mechanistically with the gut microbiota. This review will focus on the reciprocal interaction between apple components and the gut microbiota, the potential link to cardiovascular health and the possible mechanisms of action.

J Nutr. 2014 Feb;144(2):146-54.

Dietary flavonoids from modified apple reduce inflammation markers and modulate gut microbiota in mice.

Espley RV, Butts CA, Laing WA, Martell S, Smith H, McGhie TK, Zhang J, Paturi G, Hedderley D, Bovy A, Schouten HJ, Putterill J, Allan AC, Hellens RP.

Abstract

Apples are rich in polyphenols, which provide antioxidant properties, mediation of cellular processes such as inflammation, and modulation of gut microbiota. In this study we compared genetically engineered apples with increased flavonoids [myeloblastis transcription factor 10 (MYB10)] with nontransformed apples from the same genotype, "Royal Gala" (RG), and a control diet with no apple. Compared with the RG diet, the MYB10 diet contained elevated concentrations of the flavonoid subclasses anthocyanins, flavanol monomers (epicatechin) and oligomers (procyanidin B2), and flavonols (quercetin glycosides), but other plant secondary metabolites were largely unaltered. We used these apples to investigate the effects of dietary flavonoids on inflammation and gut microbiota in 2 mouse feeding trials. In trial 1, male mice were fed a control diet or diets supplemented with 20% MYB10 apple flesh and peel (MYB-FP) or RG apple flesh and peel (RG-FP) for 7 d. In trial 2, male mice were fed MYB-FP or RG-FP diets or diets supplemented with 20% MYB10 apple flesh or RG apple flesh for 7 or 21 d. In trial 1, the transcription levels of inflammation-linked genes in mice showed decreases of >2-fold for interleukin-2 receptor (Il2rb), chemokine receptor 2 (Ccr2), chemokine ligand 10 (Cxcl10), and chemokine receptor 10 (Ccr10) at 7 d for the MYB-FP diet compared with the RG-FP diet ($P < 0.05$). In trial 2, the inflammation marker prostaglandin E(2) (PGE(2)) in the plasma of mice fed the MYB-FP diet at 21 d was reduced by 10-fold ($P < 0.01$) compared with the RG-FP diet. In colonic microbiota, the number of total bacteria for mice fed the MYB-FP diet was 6% higher than for mice fed the control diet at 21 d ($P = 0.01$). In summary, high-flavonoid apple was associated with decreases in some inflammation markers and changes in gut microbiota when fed to healthy mice.

Gut. 2005 Feb;54(2):193-200.

Apple polyphenol extracts prevent damage to human gastric epithelial cells in vitro and to rat gastric mucosa in vivo.

Graziani G, D'Argenio G, Tuccillo C, Loguercio C, Ritieni A, Morisco F, Del Vecchio Blanco C, Fogliano V, Romano M.

Abstract

BACKGROUND:

Fresh fruit and vegetables exert multiple biological effects on the gastrointestinal mucosa.

AIM:

To assess whether apple extracts counteract oxidative or indomethacin induced damage to gastric epithelial cells in vitro and to rat gastric mucosa in vivo.

METHODS:

Apple extracts were obtained from freeze dried apple flesh of the "Annurca" variety. Cell damage was induced by incubating MKN 28 cells with xanthine-xanthine oxidase or indomethacin and quantitated by MTT. In vivo gastric damage was induced by indomethacin 35 mg/kg. Intracellular antioxidant activity was determined using the (2,2'-azinobis (3-ethylbenzothiazolin-6-sulfonate) method. Malondialdehyde intracellular concentration, an index of lipid peroxidation, was determined by high pressure liquid chromatography with fluorometric detection.

RESULTS:

(1) Apple extracts decreased xanthine-xanthine oxidase or indomethacin induced injury to gastric epithelial cells by 50%; (2) catechin or chlorogenic acid (the main phenolic components of apple extracts) were equally effective as apple extracts in preventing oxidative injury to gastric cells; and (3) apple extracts (i) caused a fourfold increase in intracellular antioxidant activity, (ii) prevented its decrease induced by xanthine-xanthine oxidase, (iii) counteracted xanthine-xanthine oxidase induced lipid peroxidation, and (iv) decreased indomethacin injury to the rat gastric mucosa by 40%.

CONCLUSIONS:

Apple extracts prevent exogenous damage to human gastric epithelial cells in vitro and to the rat gastric mucosa in vivo. This effect seems to be associated with the antioxidant activity of apple phenolic compounds. A diet rich in apple antioxidants might exert a beneficial effect in the prevention of gastric diseases related to generation of reactive oxygen species.

Mol Nutr Food Res. 2017 May 12.

Grape seed proanthocyanidin extract ameliorates inflammation and adiposity by modulating gut microbiota in high-fat diet mice.

Liu W, Zhao S, Wang J, Shi J, Sun Y, Wang W, Ning G, Hong J, Liu R.

Abstract

SCOPE:

Obesity and associated metabolic complications is a worldwide public health issue. Gut microbiota have been recently linked to obesity and its related inflammation. In this study, we have explored the anti-inflammatory effect of grape seed proanthocyanindin extract (GSPE) in the high-fat diet (HFD)-induced obesity and identified the contribution of the gut microbiota to GSPE effects on metabolism.

METHODS AND RESULTS:

Mice were fed a normal diet and a high-fat diet with or without GSPE (300 mg/kg body weight/day) by oral gavage for 7 weeks. Supplementation with GSPE significantly decreased plasma levels of inflammatory factors such as TNF-α, IL-6 and MCP-1, companied with ameliorated macrophage infiltration in epididymal fat and liver tissues. Furthermore, GSPE also reduced epididymal fat mass and improved insulin sensitivity. 16S rDNA analyses revealed that GSPE supplementation modulated the gut microbiota composition and certain bacteria including Clostridium XIVa, Roseburia and Prevotella. More importantly, depleting gut microbiota by antibiotics treatment abolished the beneficial effects of GSPE on inflammation and adiposity.

CONCLUSION:

Our study identifies the novel links between gut microbiota alterations and metabolic benefits by GSPE supplementation, providing possibilities for the prevention and treatment of metabolic disorders by targeting gut microbiota through a potential prebiotic agent GSPE.

Mol Nutr Food Res. 2017 Feb 20.

Chronic supplementation with dietary proanthocyanidins protects from diet-induced intestinal alterations in obese rats.

Gil-Cardoso K, Ginés I, Pinent M, Ardévol A, Arola L, Blay M, Terra X.

Abstract

SCOPE:

Increased attention has been paid to the link between altered intestinal function and elevated incidence of metabolic disorders, such as in obesity. This study investigated in obese rats the role of grape seed proanthocyanidin extract (GSPE) chronic treatment, taken in a low, moderate, or high dose, on obesity-associated intestinal alterations in response to a cafeteria diet (CAF).

METHODS AND RESULTS:

To evaluate the degree of intestinal inflammation, reactive oxygen species (ROS) production and myeloperoxidase (MPO) activity were measured as well as the expression of inflammatory-related genes. The barrier integrity was assessed by quantifying the gene expression of tight-junction components and measuring the plasma LPS. GSPE decreased the ROS levels and MPO activity, without substantial differences among the doses. The supplementation with moderate and high GSPE doses significantly decreased iNOS expression compared to the CAF group, and the same pattern was observed in the low-dose animals with respect to IL-1β expression. Moreover, the results show that GSPE significantly increases zonulin-1 expression with respect to the CAF animals.

CONCLUSION:

This study provides evidence for the ameliorative effect of a proanthocyanidin extract on high-fat/high-carbohydrate diet-induced intestinal alterations, specifically reducing intestinal inflammation and oxidative stress and suggesting a protection against a barrier defect.

Oncotarget. 2016 Dec 6;7(49):80313-80326. doi: 10.18632/oncotarget.13450.

Dietary grape seed proanthocyanidins (GSPs) improve weaned intestinal microbiota and mucosal barrier using a piglet model.

Han M, Song P, Huang C, Rezaei A, Farrar S, Brown MA, Ma X.

Abstract

Proanthocyanidins have been suggested as an effective antibiotic alternative, however their mechanisms are still unknown. The present study investigated the effects of grape seed proanthocyanidins on gut microbiota and mucosal barrier using a weaned piglet model in comparison with colistin. Piglets weaned at 28 day were randomly assigned to four groups treated with a control ration, or supplemented with 250 mg/kg proanthocyanidins, kitasamycin/colistin, or 250 mg/kg proanthocyanidins and half-dose antibiotics, respectively. On day 28, the gut chyme and tissue samples were collected to test intestinal microbiota and barrier function, respectively. Proanthocyanidins treated piglets had better growth performance and reduced diarrhea incidence ($P < 0.05$), accompanied with decreased intestinal permeability and improved mucosal morphology. Gene sequencing analysis of 16S rRNA revealed that dietary proanthocyanidins improved the microbial diversity in ileal and colonic digesta, and the most abundant OTUs belong to Firmicutes and Bacteroidetes spp.. Proanthocyanidins treatment decreased the abundance of Lactobacillaceae, and increased the abundance of Clostridiaceae in both ileal and colonic lumen, which suggests that proanthocyanidins treatment changed the bacterial composition and distribution. Administration of proanthocyanidins increased the concentration of propionic acid and butyric acid in the ileum and colon, which may activate the expression of GPR41. In addition, dietary proanthocyanidins improved the antioxidant indices in serum and intestinal mucosa, accompanied with increasing expression of barrier occludin. Our findings indicated that proanthocyanidins with half-dose colistin was equivalent to the antibiotic treatment and assisted weaned animals in resisting intestinal oxidative stress by increasing diversity and improving balance of gut microbes.

Food Funct. 2016 Apr;7(4):1959-67. doi: 10.1039/c6fo00032k.

In vitro extraction and fermentation of polyphenols from grape seeds (Vitis vinifera) by human intestinal microbiota.

Zhou L, Wang W, Huang J, Ding Y, Pan Z, Zhao Y, Zhang R, Hu B, Zeng X.

Abstract

The effects of several parameters on the extraction yield of total polyphenols from grape seeds by pressurized liquid extraction were investigated. The highest recovery of total polyphenols occurred at 80 °C within 5 min, and a single extraction allowed a recovery of more than 97% of total polyphenols. Following the purification with macroporous resin, the effects of grape polyphenols (>94.8%) on human intestinal microbiota were monitored over 36 h incubation by fluorescence in situ hybridization, and short-chain fatty acids (SCFAs) were measured by HPLC. The result showed that the grape polyphenols promoted the changes in the relevant microbial populations and shifted the profiles of SCFAs. Fermentation of grape polyphenols resulted in a significant increase in the numbers of Bifidobacterium spp. and Lactobacillus-Enterococcus group and inhibition in the growth of the Clostridium histolyticum group and the Bacteroides-Prevotella group, with no significant effect on the population of total bacteria. The findings suggest that grape polyphenols have potential prebiotic effects on modulating the gut microbiota composition and generating SCFAs that contribute to the improvements of host health.

Curr Obes Rep. 2015 Dec;4(4):389-400.

Gut Microbiota Dysbiosis in Obesity-Linked Metabolic Diseases and Prebiotic Potential of Polyphenol-Rich Extracts.

Anhê FF, Varin TV, Le Barz M, Desjardins Y, Levy E, Roy D, Marette A.

Abstract

Trillions of microorganisms inhabit the human body, strongly colonizing the gastro-intestinal tract and outnumbering our own cells. High-throughput sequencing techniques and new bioinformatic tools have enabled scientists to extend our knowledge on the relationship between the gut microbiota and host's physiology. Disruption of the ecological equilibrium in the gut (i.e., dysbiosis) has been associated with several pathological processes, including obesity and its related comorbidities, with diet being a strong determinant of gut microbial balance. In this review, we discuss the potential prebiotic effect of polyphenol-rich foods and extracts and how they can reshape the gut microbiota, emphasizing the novel role of the mucin-degrading bacterium Akkermansia muciniphila in their metabolic benefits.

Food Funct. 2014 Oct;5(10):2558-63.

Grape seed extract improves epithelial structure and suppresses inflammation in ileum of IL-10-deficient mice.

Yang G, Wang H, Kang Y, Zhu MJ.

Abstract

Defect in intestinal epithelial structure is a critical etiological factor of several intestinal diseases such as inflammatory bowel disease. The objective of this study was to evaluate the effect of grape seed extract (GSE), which contains a mixture of polyphenols, on ileal mucosal structure and inflammation in interleukin (IL)-10-deficient mice, a common model for studying inflammatory bowel disease. Wild-type and IL-10-deficient mice were fed GSE at 0 or 1% (based on dry feed weight) for 16 weeks. GSE supplementation decreased crypt depth and increased ($P < 0.05$) the ratio of villus/crypt length in the terminal ileum. Consistently, the dietary GSE decreased ($P < 0.05$) proliferation and enhanced ($P < 0.05$) differentiation of epithelial cells. These changes in gut epithelium were associated with the suppression of nuclear factor kappa-light-chain-enhancer of activated B-cell (NF-κB) signaling. Furthermore, compared with WT mice, IL-10 deletion promoted beclin-1 and AMPK expression, both of which were decreased to normal by GSE supplementation. These changes were associated with alterations in epithelial barrier function as indicated by reduced pore forming claudin-2 protein expression and increased barrier forming claudin-1 protein expression in the ileum of GSE supplemented mice. In summary, our data indicates that GSE exerts protective effects to the ileal epithelial structure in IL-10-deficient mice possibly through the suppression of inflammatory response.

Gut Liver. 2013 May;7(3):282-9.

Gastroprotective Effects of Grape Seed Proanthocyanidin Extracts against Nonsteroid Anti-Inflammatory Drug-Induced Gastric Injury in Rats.

Kim TH, Jeon EJ, Cheung DY, Kim CW, Kim SS, Park SH, Han SW, Kim MJ, Lee YS, Cho ML, Chang JH, Min JK, Kim JI.

Abstract

BACKGROUND/AIMS:

To investigate the gastroprotective effects of grape seed proanthocyanidin extracts (GSPEs) against nonsteroid anti-inflammatory drug (NSAID)-induced gastric mucosal injury in rats.

METHODS:

Sprague-Dawley rats were randomly allocated to the normal control, indomethacin, low-dose GSPE, high-dose GSPE and misoprostol groups. All groups except the normal control group received pretreatment drugs for 6 consecutive days. On the 5th and 6th day, indomethacin was administered orally to all groups except for normal control group. The microscopic features of injury were analyzed. The levels of gastric mucosal glutathione, gastric mucosal prostaglandin E2 (PGE2), and proinflammatory cytokines were investigated.

RESULTS:

The total areas of ulceration in the GSPE and misoprostol groups were significantly decreased compared with the indomethacin group ($p<0.05$). However, a difference in ulcer formation among the drug treatment groups was not observed. Meanwhile, the glutathione levels in the high-dose GSPE group were higher than those of both the indomethacin and misoprostol groups ($p<0.05$) and were similar to those of the normal control group. Additionally, there was no difference among the groups in the levels of gastric mucosal PGE2 and proinflammatory cytokines.

CONCLUSIONS:

High-dose GSPE has a strong protective effect against NSAID-induced gastric mucosal injury, which may be associated with the antioxidant effects of GSPE.

Can J Physiol Pharmacol. 2010 Sep;88(9):888-98. doi: 10.1139/y10-071.

Effects of proanthocyanidins from grape seed on treatment of recurrent ulcerative colitis in rats.

Wang YH, Yang XL, Wang L, Cui MX, Cai YQ, Li XL, Wu YJ.

Abstract

The aim of the present study was to investigate the therapeutic effect and mechanism of proanthocyanidins from grape seed (GSPE) in the treatment of recurrent ulcerative colitis (UC) in rats. To induce recurrent colitis, rats were instilled with 2,4,6-trinitrobenzenesulfonic acid (TNBS) (80 mg/kg) into the colon through the cannula in the first induced phase, and then the rats were instilled a second time with TNBS (30 mg/kg) into the colon on the sixteenth day after the first induction UC. Rats were intragastrically administered GSPE (200 mg/kg) per day for 7 days after twice-induced colitis by TNBS. Sulfasalazine at 500 mg/kg was used as a positive control drug. Rats were killed 7 days after GSPE treatment. The colonic injury and inflammation were assessed by macroscopic and macroscopic damage scores, colon weight/length ratio (mg/cm), and myeloperoxidase activity. Then, superoxide dismutase, glutathione peroxidase, inducible nitric oxide synthase (iNOS) activities, and the levels of malonyldialdehyde, glutathione, and nitric oxide in serum and colonic tissues were measured. Compared with the recurrent UC group, GSPE treatment facilitated recovery of pathologic changes in the colon after induction of recurrent colitis, as demonstrated by reduced colonic weight/length ratio and macroscopic and microscopic damage scores. The myeloperoxidase and iNOS activities with malonyldialdehyde and nitric oxide levels in serum and colon tissues of colitis rats were significantly decreased in the GSPE group compared with those in the recurrent UC group. In addition, GSPE treatment was associated with notably increased superoxide dismutase, glutathione peroxidase activities, and glutathione levels of colon tissues and serum of rats. GSPE exerted a protective effect on recurrent colitis in rats by modifying the inflammatory response, inhibiting inflammatory cell infiltration and antioxidation damage, promoting damaged tissue repair to improve colonic oxidative stress, and inhibiting colonic iNOS activity to reduce the production of nitric oxide.

Food Funct. 2016 Apr;7(4):1788-96. doi: 10.1039/c5fo01096a.

Impact of increasing fruit and vegetables and flavonoid intake on the human gut microbiota.

Klinder A, Shen Q, Heppel S, Lovegrove JA, Rowland I, Tuohy KM.

Abstract

Epidemiological studies have shown protective effects of fruits and vegetables (F&V) in lowering the risk of developing cardiovascular diseases (CVD) and cancers. Plant-derived dietary fibre (non-digestible polysaccharides) and/or flavonoids may mediate the observed protective effects particularly through their interaction with the gut microbiota. The aim of this study was to assess the impact of fruit and vegetable (F&V) intake on gut microbiota, with an emphasis on the role of flavonoids, and further to explore relationships between microbiota and factors associated with CVD risk. In the study, a parallel design with 3 study groups, participants in the two intervention groups representing high-flavonoid (HF) and low flavonoid (LF) intakes were asked to increase their daily F&V intake by 2, 4 and 6 portions for a duration of 6 weeks each, while a third (control) group continued with their habitual diet. Faecal samples were collected at baseline and after each dose from 122 subjects. Faecal bacteria enumeration was performed by fluorescence in situ hybridisation (FISH). Correlations of dietary components, flavonoid intake and markers of CVD with bacterial numbers were also performed. A significant dose X treatment interaction was only found for Clostidium leptum-Ruminococcus bromii/flavefaciens with a significant increase after intake of 6 additional portions in the LF group. Correlation analysis of the data from all 122 subjects independent from dietary intervention indicated an inhibitory role of F&V intake, flavonoid content and sugars against the growth of potentially pathogenic clostridia. Additionally, we observed associations between certain bacterial populations and CVD risk factors including plasma TNF-α, plasma lipids and BMI/waist circumference.

Curr Obes Rep. 2015 Dec;4(4):389-400.

Gut Microbiota Dysbiosis in Obesity-Linked Metabolic Diseases and Prebiotic Potential of Polyphenol-Rich Extracts.

Anhê FF, Varin TV, Le Barz M, Desjardins Y, Levy E, Roy D, Marette A.

Abstract

Trillions of microorganisms inhabit the human body, strongly colonizing the gastro-intestinal tract and outnumbering our own cells. High-throughput sequencing techniques and new bioinformatic tools have enabled scientists to extend our knowledge on the relationship between the gut microbiota and host's physiology. Disruption of the ecological equilibrium in the gut (i.e., dysbiosis) has been associated with several pathological processes, including obesity and its related comorbidities, with diet being a strong determinant of gut microbial balance. In this review, we discuss the potential prebiotic effect of polyphenol-rich foods and extracts and how they can reshape the gut microbiota, emphasizing the novel role of the mucin-degrading bacterium Akkermansia muciniphila in their metabolic benefits.

Gut. 2016 Feb;65(2):330-9.

The gut microbiota and host health: a new clinical frontier.

Marchesi JR, Adams DH, Fava F, Hermes GD, Hirschfield GM, Hold G, Quraishi MN, Kinross J, Smidt H, Tuohy KM, Thomas LV, Zoetendal EG, Hart A.

Abstract

Over the last 10-15 years, our understanding of the composition and functions of the human gut microbiota has increased exponentially. To a large extent, this has been due to new 'omic' technologies that have facilitated large-scale analysis of the genetic and metabolic profile of this microbial community, revealing it to be comparable in influence to a new organ in the body and offering the possibility of a new route for therapeutic intervention. Moreover, it might be more accurate to think of it like an immune system: a collection of cells that work in unison with the host and that can promote health but sometimes initiate disease. This review gives an update on the current knowledge in the area of gut disorders, in particular metabolic syndrome and obesity-related disease, liver disease, IBD and colorectal cancer. The potential of manipulating the gut microbiota in these disorders is assessed, with an examination of the latest and most relevant evidence relating to antibiotics, probiotics, prebiotics, polyphenols and faecal microbiota transplantation.

Clin Ther. 2015 May 1;37(5):984-95.

Gut-Microbiota-Brain Axis and Its Effect on Neuropsychiatric Disorders With Suspected Immune Dysregulation.

Petra AI, Panagiotidou S, Hatziagelaki E, Stewart JM, Conti P, Theoharides TC.

Abstract

PURPOSE:

Gut microbiota regulate intestinal function and health. However, mounting evidence indicates that they can also influence the immune and nervous systems and vice versa. This article reviews the bidirectional relationship between the gut microbiota and the brain, termed the microbiota-gut-brain (MGB) axis, and discusses how it contributes to the pathogenesis of certain disorders that may involve brain inflammation.

METHODS:

Articles were identified with a search of Medline (starting in 1980) by using the key words anxiety, attention-deficit hypersensitivity disorder (ADHD), autism, cytokines, depression, gut, hypothalamic-pituitary-adrenal (HPA) axis, inflammation, immune system, microbiota, nervous system, neurologic, neurotransmitters, neuroimmune conditions, psychiatric, and stress.

FINDINGS:

Various afferent or efferent pathways are involved in the MGB axis. Antibiotics, environmental and infectious agents, intestinal neurotransmitters/neuromodulators, sensory vagal fibers, cytokines, and essential metabolites all convey information to the central nervous system about the intestinal state. Conversely, the hypothalamic-pituitary-adrenal axis, the central nervous system regulatory areas of satiety, and neuropeptides released from sensory nerve fibers affect the gut microbiota composition directly or through nutrient availability. Such interactions seem to influence the pathogenesis of a number of disorders in which inflammation is implicated, such as mood disorder, autism-spectrum disorders, attention-deficit hypersensitivity disorder, multiple sclerosis, and obesity.

IMPLICATIONS:

Recognition of the relationship between the MGB axis and the neuroimmune systems provides a novel approach for better understanding and management of these disorders. Appropriate preventive measures early in life or corrective measures such as use of psychobiotics, fecal microbiota transplantation, and flavonoids are discussed.

Biomed Res Int. 2015;2015:850902.

A survey of modulation of gut microbiota by dietary polyphenols.

Dueñas M, Muñoz-González I, Cueva C, Jiménez-Girón A, Sánchez-Patán F, Santos-Buelga C, Moreno-Arribas MV, Bartolomé B.

Abstract

Dietary polyphenols present in a broad range of plant foods have been related to beneficial health effects. This review aims to update the current information about the modulation of the gut microbiota by dietary phenolic compounds, from a perspective based on the experimental approaches used. After referring to general aspects of gut microbiota and dietary polyphenols, studies related to this topic are presented according to their experimental design: batch culture fermentations, gastrointestinal simulators, animal model studies, and human intervention studies. In general, studies evidence that dietary polyphenols may contribute to the maintenance of intestinal health by preserving the gut microbial balance through the stimulation of the growth of beneficial bacteria (i.e., lactobacilli and bifidobacteria) and the inhibition of pathogenic bacteria, exerting prebiotic-like effects. Combination of in vitro and in vivo models could help to understand the underlying mechanisms in the polyphenols-microbiota-host triangle and elucidate the implications of polyphenols on human health. From a technological point of view, supplementation with rich-polyphenolic stuffs (phenolic extracts, phenolic-enriched fractions, etc.) could be an effective option to improve health benefits of functional foods such as the case of dairy fermented foods.

Eur J Nutr. 2015 Apr;54(3):325-41.

Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: a review.

Duda-Chodak A, Tarko T, Satora P, Sroka P.

Abstract

The intestinal microbiome plays an important role in the metabolism of chemical compounds found within food. Bacterial metabolites are different from those that can be generated by human enzymes because bacterial processes occur under anaerobic conditions and are based mainly on reactions of reduction and/or hydrolysis. In most cases, bacterial metabolism reduces the activity of dietary compounds; however, sometimes a specific product of bacterial transformation exhibits enhanced properties. Studies on the metabolism of polyphenols by the intestinal microbiota are crucial for understanding the role of these compounds and their impact on our health. This review article presents possible pathways of polyphenol metabolism by intestinal bacteria and describes the diet-derived bioactive metabolites produced by gut microbiota, with a particular emphasis on polyphenols and their potential impact on human health. Because the etiology of many diseases is largely correlated with the intestinal microbiome, a balance between the host immune system and the commensal gut microbiota is crucial for maintaining health. Diet-related and age-related changes in the human intestinal microbiome and their consequences are summarized in the paper.

Mech Ageing Dev. 2014 Mar-Apr;136-137:59-69.

Cognitive decline, dietary factors and gut-brain interactions.

Caracciolo B, Xu W, Collins S, Fratiglioni L.

Abstract

Cognitive decline in elderly people often derives from the interaction between aging-related changes and age-related diseases and covers a large spectrum of clinical manifestations, from intact cognition through mild cognitive impairment and dementia. Epidemiological evidence supports the hypothesis that modifiable lifestyle-related factors are associated with cognitive decline, opening new avenues for prevention. Diet in particular has become the object of intense research in relation to cognitive aging and neurodegenerative disease. We reviewed the most recent findings in this rapidly expanding field. Some nutrients, such as vitamins and fatty acids, have been studied longer than others, but strong scientific evidence of an association is lacking even for these compounds. Specific dietary patterns, like the Mediterranean diet, may be more beneficial than a high consumption of single nutrients or specific food items. A strong link between vascular risk factors and dementia has been shown, and the association of diet with several vascular and metabolic diseases is well known. Other plausible mechanisms underlying the relationship between diet and cognitive decline, such as inflammation and oxidative stress, have been established. In addition to the traditional etiological pathways, new hypotheses, such as the role of the intestinal microbiome in cognitive function, have been suggested and warrant further investigation.

J Proteome Res. 2012 Oct 5;11(10):4781-90.

Metabolomics view on gut microbiome modulation by polyphenol-rich foods.

Moco S, Martin FP, Rezzi S.

Abstract

Health is influenced by genetic, lifestyle, and diet determinants; therefore, nutrition plays an essential role in health management. Still, the substantiation of nutritional health benefits is challenged by the intrinsic macro- and micronutrient complexity of foods and individual responses. Evidence of healthy effects of food requires new strategies not only to stratify populations according to their metabolic requirements but also to predict and measure individual responses to dietary intakes. The influence of the gut microbiome and its interaction with the host is pivotal to understand nutrition and metabolism. Thus, the modulation of the gut microbiome composition by alteration of food habits has potentialities in health improvement or even disease prevention. Dietary polyphenols are naturally occurring constituents in vegetables and fruits, including coffee and cocoa. They are commonly associated to health benefits, although mechanistic evidence in vivo is not yet fully understood. Polyphenols are extensively metabolized by gut bacteria into a complex series of end-products that support a significant effect on the functional ecology of symbiotic partners that can affect the host physiology. This review reports recent nutritional metabolomics inspections of gut microbiota-host metabolic interactions with a particular focus on the cometabolism of cocoa and coffee polyphenols.

J Agric Food Chem. 2012 Sep 12;60(36):8776-82.

Up-regulating the human intestinal microbiome using whole plant foods, polyphenols, and/or fiber.

Tuohy KM, Conterno L, Gasperotti M, Viola R.

Abstract

Whole plant foods, including fruit, vegetables, and whole grain cereals, protect against chronic human diseases such as heart disease and cancer, with fiber and polyphenols thought to contribute significantly. These bioactive food components interact with the gut microbiota, with gut bacteria modifying polyphenol bioavailability and activity, and with fiber, constituting the main energy source for colonic fermentation. This paper discusses the consequences of increasing the consumption of whole plant foods on the gut microbiota and subsequent implications for human health. In humans, whole grain cereals can modify fecal bacterial profiles, increasing relative numbers of bifidobacteria and lactobacilli. Polyphenol-rich chocolate and certain fruits have also been shown to increase fecal bifidobacteria. The recent FLAVURS study provides novel information on the impact of high fruit and vegetable diets on the gut microbiota. Increasing whole plant food consumption appears to up-regulate beneficial commensal bacteria and may contribute toward the health effects of these foods.

Fitoterapia. 2011 Jan;82(1):53-66.

The intestinal microbiome: a separate organ inside the body with the metabolic potential to influence the bioactivity of botanicals.

Possemiers S, Bolca S, Verstraete W, Heyerick A.

Abstract

For many years, it was believed that the main function of the large intestine was the resorption of water and salt and the facilitated disposal of waste materials. However, this task definition was far from complete, as it did not consider the activity of the microbial content of the large intestine. Nowadays it is clear that the complex microbial ecosystem in our intestines should be considered as a separate organ within the body, with a metabolic capacity which exceeds the liver with a factor 100. The intestinal microbiome is therefore closely involved in the first-pass metabolism of dietary compounds. This is especially true for botanical supplements, which are now marketed for various health applications. Being of natural origin, their structural building blocks, such as polyphenols, are often highly recognized by the human and especially the intestinal microbial metabolism machinery. Intensive metabolism results in often low circulating levels of the original products, with the consequence that final health effects of botanicals are often related to specific active metabolites which are produced in the body rather than being related to the product's original composition. Understanding how such metabolic processes contribute to the in situ exposure is therefore crucial for the proper interpretation of biological responses. A multidisciplinary approach, characterizing the food and phytochemical intake as well as the metabolic potency of the gut microbiota, while measuring biomarkers of both exposure and response in target tissues, is therefore of critical importance. With polyphenol metabolism as example, this review describes how the incorporation of microbial metabolism as an important variable in the evaluation of the final bioactivity of botanicals strongly increases the relevance and predictive value of the outcome. Moreover, knowledge about intestinal processes may offer innovative strategies for targeted product development.

Digestive Performance Blend – Selected Background Documents

Eur Rev Med Pharmacol Sci. 2016;20(1):146-9.

The effect of ginger (Zingiber officinalis) and artichoke (Cynara cardunculus) extract supplementation on gastric motility: a pilot randomized study in healthy volunteers.

Lazzini S, Polinelli W, Riva A, Morazzoni P, Bombardelli E.

Abstract

OBJECTIVE:

Prodigest® is the standardized combination of artichoke and ginger extracts. This combination was safe and effective in the treatment of functional dyspepsia. However, further evidence could be useful to shed new lights on the effect of Prodigest® on gastric motility. This pilot randomized study on healthy volunteers investigates the prokinetic activity of Prodigest®.

SUBJECTS AND METHODS:

This was a randomized, cross-over study in healthy volunteers comparing Prodigest® versus placebo. Eleven healthy volunteers were enrolled. Each participant underwent two evaluations, at a 7-day interval. Ten minutes before the main meal, the baseline area of gastric volume was determined by ultrasonography. The subject was then given one Prodigest® or placebo capsule and, then consumed a standardized meal. One hour after the meal, the gastric volume was measured again. Two weeks after the second evaluation, three subjects repeated the above-mentioned procedures taking two capsules of Prodigest®.

RESULTS:

The mean gastric area at baseline was 3.2 ± 0.5 cm(2); after the meal, this figure was 8.4 ± 0.7 cm(2) with Prodigest® and 11.0 ± 1.5 cm2 with placebo ($p<0.001$). The after-meal gastric area was significantly smaller, with a -24% difference, following the combination of extracts, as compared with placebo ($p<0.001$). The effect of two capsules of Prodigest® seems to be more evident but due to the very small number of the patients sample further clinical data are necessary before confirming the dose-related effects.

CONCLUSIONS:

This pilot study shows that Prodigest®, a standardized extract of ginger and artichoke, significantly promotes gastric emptying in healthy volunteers without being associated with notable adverse effects.

Evid Based Complement Alternat Med. 2015;2015:915087.

The Effect of Ginger (Zingiber officinalis) and Artichoke (Cynara cardunculus) Extract Supplementation on Functional Dyspepsia: A Randomised, Double-Blind, and Placebo-Controlled Clinical Trial.

Giacosa A, Guido D, Grassi M, Riva A, Morazzoni P, Bombardelli E, Perna S, Faliva MA, Rondanelli M.

Abstract

Objective. Functional dyspepsia (FD) is a frequent clinical finding in western world. The aim of this study is to compare the efficacy of a ginger and artichoke supplementation versus placebo in the treatment of FD. Methods. A prospective multicentre, double blind, randomized, placebo controlled, parallel-group comparison of the supplement and placebo over a period of 4 weeks was performed. Two capsules/day were supplied (before lunch and dinner) to 126 FD patients (supplementation/placebo: 65/61). Results. After 14 days of treatment, only supplementation group (SG) showed a significant amelioration (SG: α S = +1.195 MCA score units (u), P = 0.017; placebo: α P = +0.347 u, P = 0.513). The intercept (α) resulted to be significantly higher in SG than in placebo (α S - α P = +0.848 u, P < 0.001). At the end of the study, the advantage of SG versus placebo persists without variation (β S - β P = +0.077 u, P = 0.542). In SG, a significant advantage is observed for nausea (β S - β P = -0.398 u, P < 0.001), epigastric fullness (β S - β P = -0.241, P < 0.001), epigastric pain (β S - β P = -0.173 u, P = 0.002), and bloating (β S - β P = -0.167 u, P = 0.017). Conclusions. The association between ginger and artichoke leaf extracts appears safe and efficacious in the treatment of FD and could represent a promising treatment for this disease.